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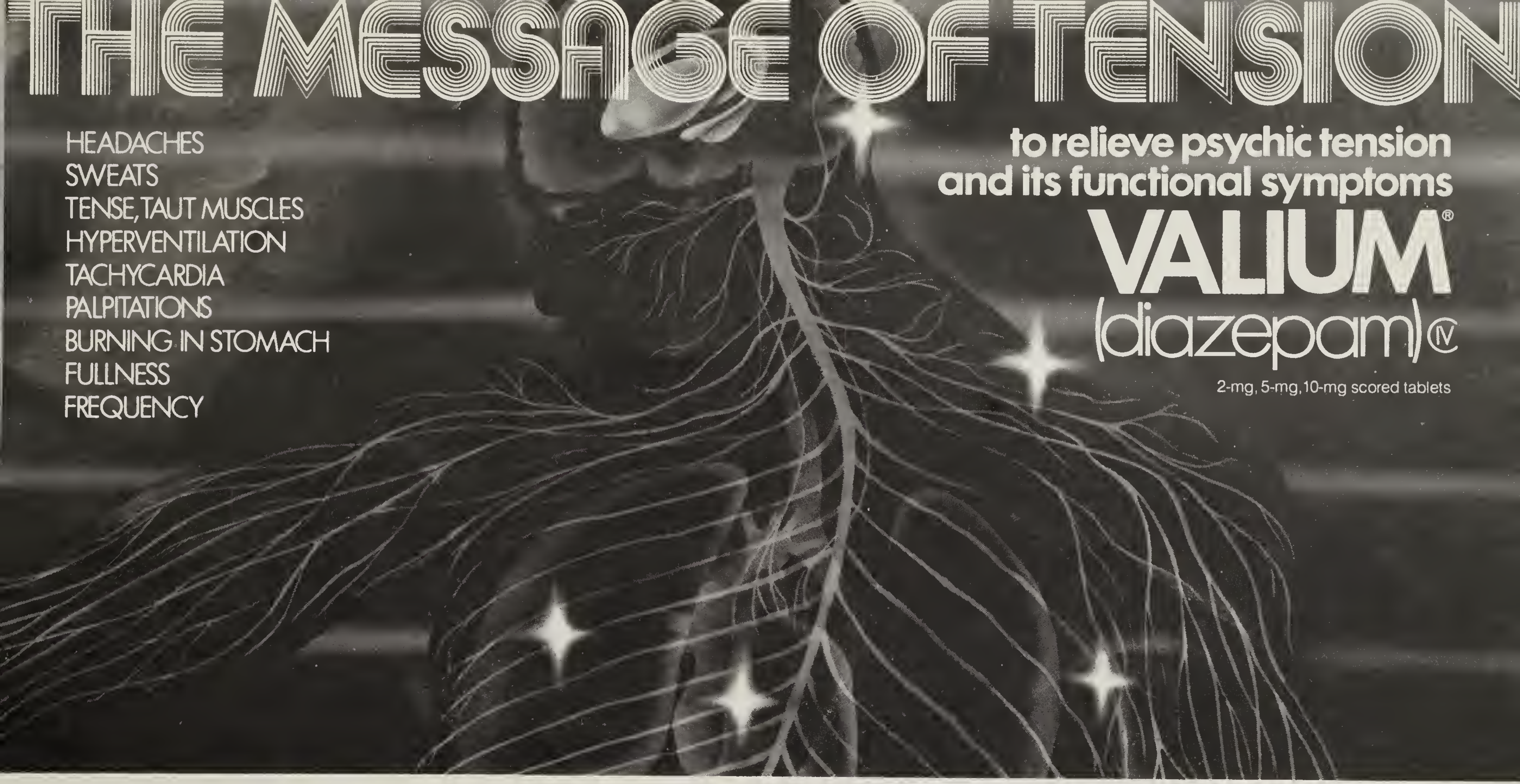

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Before prescribing, please consult complete product information, a summary of which follows:
Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome, convulsive disorders (not for sole therapy).
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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.
Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**
Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.
Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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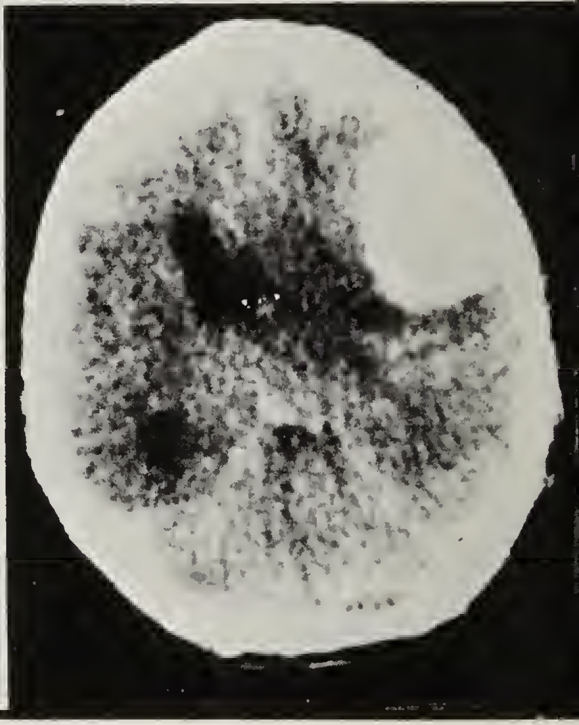

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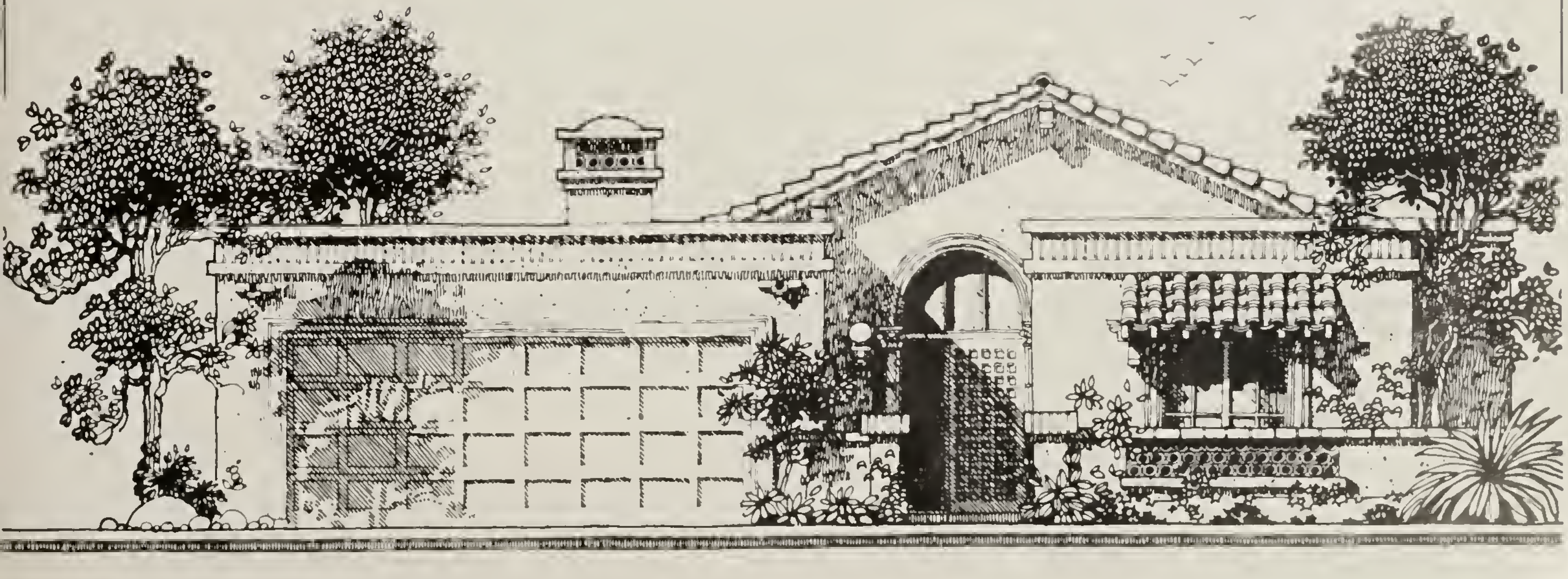

What you ~~should~~ must know about the new Arizona Drug Substitution law

As of January 1, 1979, the state legislature dramatically changed the lawful way of prescribing drugs and of writing a prescription. Until now, writing the brand name of a drug on the prescription was enough to ensure that the brand-name drug would indeed be dispensed. Now that no longer suffices. Unless the physician takes the necessary extra steps, for many drugs the pharmacist may substitute an "equivalent" generic drug where available.

Key points for the physician in writing prescriptions

- "Every prescription form in the state of Arizona should contain two signature lines for the prescriber."
- "The right side of the prescription form shall contain under the signature line the phrase 'substitution permissible.' The left side shall contain under the signature line the phrase 'dispense as written.'"

NOTE:

- "In the instance of an oral prescription, the registrant shall note the prescriber's instructions on the face of the prescription."
- "When a substitution is made . . . the registrant shall include on the label of the container the name of the dispensed drug and the name of the manufacturer of the dispensed generic drug."

℞

dispense as written	substitution permissible

J8MK06

The decisions the physician must make

The physician should acquaint himself with the newly mandated prescription form illustrated on the preceding page. This form requires a distinct change from the way he has previously written prescriptions.

There are now *two* lines for the prescriber's signature. The prescription may be filled generically unless the physician signs on the line stating "dispense as written." Special note should be made of the position of this line in the lower *left* of the prescription form rather than on the right, where the physician has customarily signed prescriptions. Only by signing on the left side can he ensure that the brand-name drug will be dispensed.

If the physician elects to permit substitution, he must indicate this by signing on the line marked "substitution permissible." This line is in the lower right hand corner of the prescription form.

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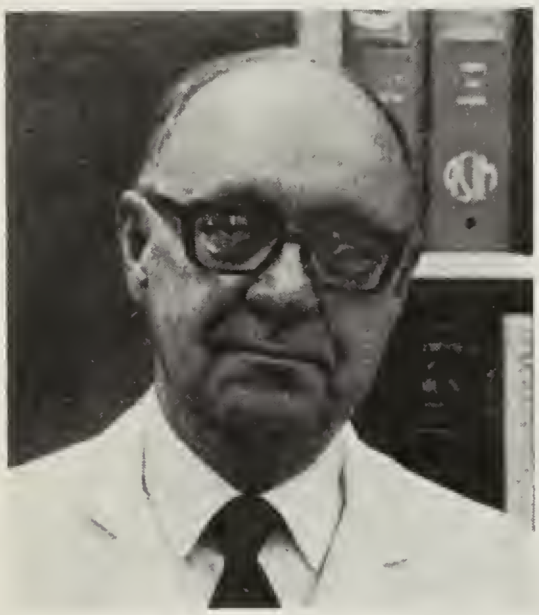

More and more physicians today are beginning to realize the extent of the economic influence they have, and are finding ways of holding costs down.

A number of studies show that the more physicians *know* about costs, the more they try to *reduce* them.* And this reduction can be done without reducing the quality of care to the patient.

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More physicians today realize what a tough problem we're all faced with. They know this is a challenge for medicine. And that physicians are in the best position to deal with and solve the problem.

**PATIENT CARE Magazine—Outlook 1977, "Face-Off: Cost Containment vs. Chaos," January 1, 1977.*
Lyle CB, et al. "Practice habits in a group of eight internists," ANNALS OF INTERNAL MEDICINE 84 (May 1976), 594-601.
Schroeder SA, et al. "Use of laboratory tests and pharmaceuticals: variation among physicians and effect of cost audit on subsequent use," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 225 (Aug. 20, 1973), 969-73.

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So it is not surprising that in this short period Motrin has become the most frequently prescribed alternative to aspirin. Motrin relieves joint pain and inflammation as effectively as indomethacin or aspirin, but causes significantly fewer CNS and milder GI reactions.
However, gastrointestinal bleeding, sometimes severe, has been associated with Motrin, aspirin, indomethacin, and other nonsteroidal antiarthritic agents.

*The safety and effectiveness of Motrin have not been established in patients with Functional Class IV rheumatoid arthritis (incapacitated, largely or wholly bedridden, or confined to wheelchair; little or no self-care).

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Motrin 400 TABLETS mg
ibuprofen, Upjohn

The confidence that comes from experience—
one more reason to prescribe Motrin.

Please turn page for a brief summary of prescribing information.

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Motrin 400 mg TABLETS
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Indications and Usage: Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Contraindications: Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

Warnings: Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.

Drug interactions. *Aspirin* used concomitantly may decrease Motrin blood levels. *Coumarin:* Bleeding has been reported in patients taking Motrin and coumarin.

Pregnancy and nursing mothers: Motrin should not be taken during pregnancy or by nursing mothers.

Adverse Reactions

Incidence greater than 1%

Gastrointestinal: The most frequent type of adverse reaction occurring with Motrin (ibuprofen) is gastrointestinal (4% to 16%). This includes nausea*, epigastric pain*, heartburn*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness*, headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

Incidence: Unmarked 1% to 3%; *3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

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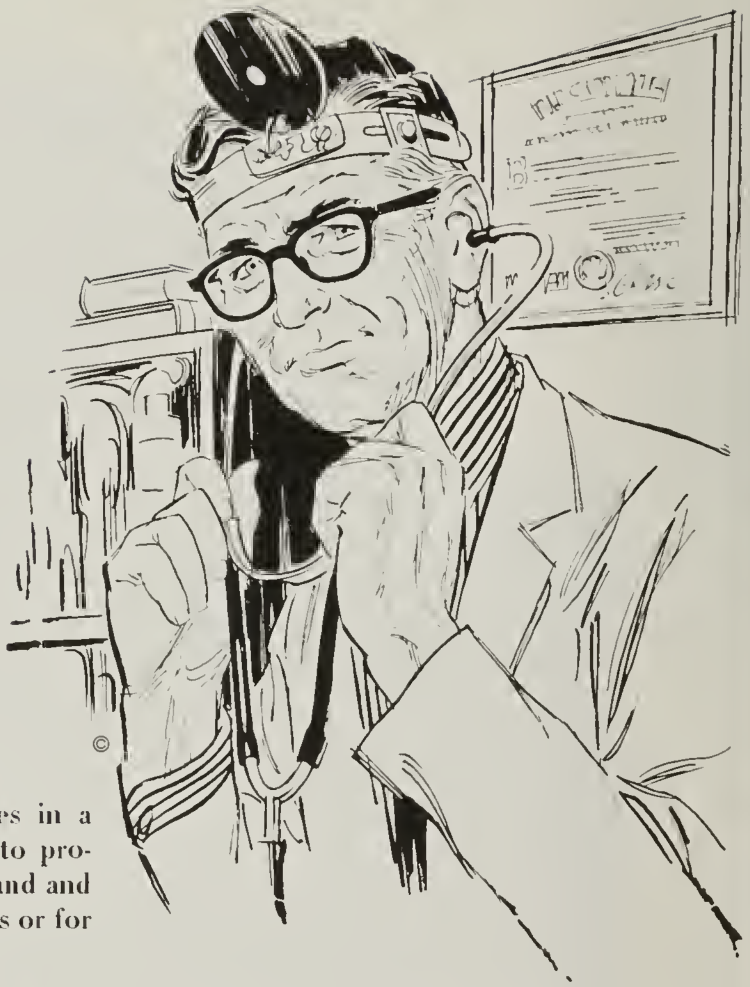

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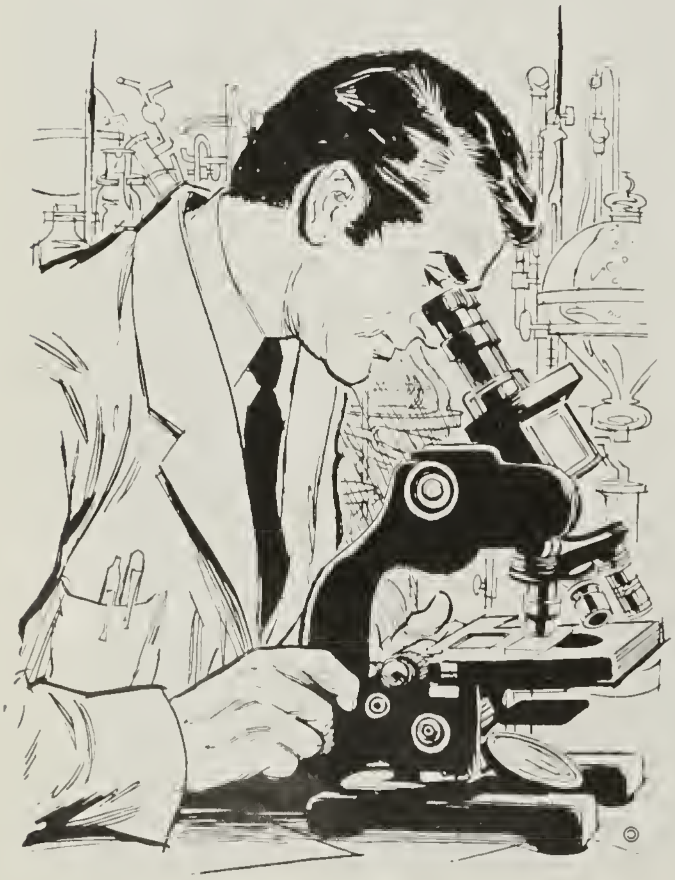

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A Multiple Disciplinary Problem
Part I

Robert G. Volz, M.D.
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Jack M. Layton, M.D.

Arthritis is a term that covers many clinical entities from the trivial to the devastating. The good news is that it seldom kills anyone; the bad news is that it seldom goes away. Chronicity is the hallmark.

In the United States, one person in ten, over 22 million people, suffers with some form of arthritis. Five million are in constant pain, one million are totally disabled. The dollar cost is staggering. Four years ago, Congress in an effort to overcome this major problem passed the Arthritis Act of 1975, creating an arthritis commission to study the problem and develop new programs to comb arthritis. The result has been the designation of fourtee new centers of research and education in arthritis which Tucson is one.

It seems appropriate, then, that the Dean's Clinic Rounds consider rheumatoid disease, a disease which di not exist two hundred years ago, at least in Wester Civilization, and which today is the most devastating an one of the most common types of arthritis with a incidence of nearly one percent of the general populatio It is our intent to emphasize the multiple disciplir approach to the care of the arthritic as it follows th

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From: U of A Health Sciences Center, Tucson, AZ 85724. Reprint requests to Dr. Volz.

TABLE 1

DIAGNOSTIC CRITERIA FOR THE DIAGNOSIS OF RHEUMATOID DISEASE

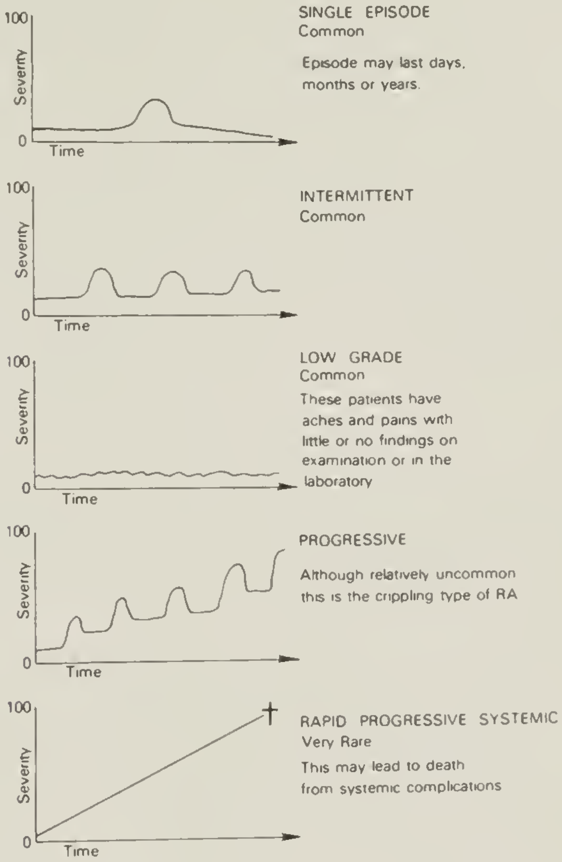
1. Morning stiffness (one hour or more).
2. Pain on motion or tenderness of the joint lasting six weeks.
3. Swelling of one joint lasting six weeks.
4. Swelling of one other joint at the same time.
5. Symmetric joint swelling (exclude DIP).
6. Subcutaneous nodules.
7. Typical X-ray changes.
8. Positive rheumatoid factor.
9. Poor mucin clot-synovial fluid.
10. Characteristic synovial histology.
11. Characteristic nodule histology.

complicated disease requires complicated therapy. But, it is well to remind ourselves that most of us train in a narrow discipline and form habits which may give us difficulty recalling the help that is available from others. Knowing where to find and how to use this help is our theme. Our patient for today is the most essential member of this team as he has spent more time contemplating the meaning of arthritis than any of us.

Patient Presentation

J. H., a 55-year-old male, was well until 1964 when he experienced the sudden onset of severe pain in multiple joints. As a partner in a small home construction firm, the patient continued to work for approximately six months until he became unable to dress or care for himself. Since then the patient has required the assistance of his wife for most activities of daily living. The patient's medical treatment has been extensive and varied and has included such medications as aspirin, indomethacin, phenylbutazone, ibuprofen, intra-articular and systemic steriods, and gold. He has had twenty-two surgical procedures, including median and ulnar nerve decompressions, bilateral metatarsophalangeal resections, and bilateral total knee replacement. Although remission of symptoms was noted with gold therapy, this medication was discontinued because of pruritis and persistent proteinuria. Steriod induced osteoporosis with vertebral body compression fractures requiring hospitalization was recently experienced. In an attempt to withdraw him from steroids, penicillamine was begun several weeks ago. Present medications include aspirin, acetaminophen, prednisone 4 mg. daily, calcium, Vitamin D, and antacids. Despite this therapy, persistent morning stiffness and the inability to walk farther than 100 yards because of fatigue is noted.

J. H.'s wife has been unemployed since 1965 because of the demand of caring for her husband. J. H. receives social security and V. A. pensions. His two daughters have completed college educations financed by government scholarships and loans.



SINGLE EPISODE
Common
Episode may last days, months or years.

INTERMITTENT
Common

LOW GRADE
Common
These patients have aches and pains with little or no findings on examination or in the laboratory

PROGRESSIVE
Although relatively uncommon this is the crippling type of RA

RAPID PROGRESSIVE SYSTEMIC
Very Rare
This may lead to death from systemic complications

FIGURE 1*

*From: Fritz, W. L., Paxinos, J. and Gall, E. P. "Rational Use of New Nonsteroidal Anti-Inflammatory Drugs," *Drug Therapy*, May 1978.

Clinical Manifestations and Medical Treatment

Eric P. Gall, M.D.

The diagnosis of rheumatoid arthritis is established clinically by applying the eleven criteria developed by the American Rheumatism Association (Table 1).[1] The diagnostic certainty of rheumatoid arthritis is proportional to the number of criteria present; the presence of seven criteria identifies the patient as having classic disease, five as definite, three as probable, and two as possible. In spite of this schematic attempt to correctly identify the patient with rheumatoid arthritis, long-term follow-up may prove the diagnosis incorrect as symptoms disappear or another type of arthritis develops. Generally, the onset and course of rheumatoid disease can be quite variable (Figure 1).[2] The most common presentation represents a single episode of symptoms. Rarely is the progressive type of disease observed; a fact which should be borne in mind when initially educating the patient about the prognosis.

The clinical distribution of skeletal symptoms can also be quite variable, but a symmetrical pattern of joint involvement is most commonly seen. The onset of symptoms most frequently occurs during the winter months; a low grade familial predilection to the disease is

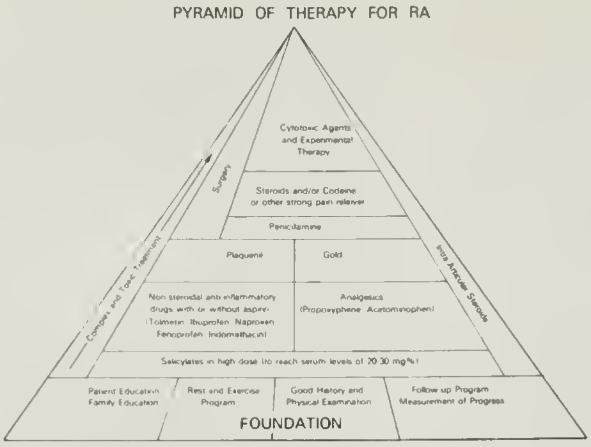

PYRAMID OF THERAPY FOR RA
Cytotoxic Agents and Experimental Therapy
Surgery
Steroids and/or Codeine or other strong pain reliever
Penicillamine
Complex and Toxic Treatment
Plaquenil
Gold
Intra Articular Steroids
Non steroidal anti-inflammatory drugs with or without aspirin (Tolmetin Ibuprofen Naproxen Fenoprofen Indomethacin)
Analgesics (Propoxyphene Acetominophen)
Salicylates in high dose (to reach serum levels of 20-30 mg%)
Patient Education Family Education
Rest and Exercise Program
Good History and Physical Examination
Follow up Program Measurement of Progress
FOUNDATION

FIGURE 2*

*From: Fritz, W. L., Paxinos, J. and Gall, E. P. "Rational Use of New Nonsteroidal Anti-Inflammatory Drugs," *Drug Therapy,* May 1978.

occasionally noted. Females exhibit three-fold increase in the incidence once the diagnosis is firmly established. Yet, at the time of initial symptoms, male and female patients are approximately equal. These facts tend to suggest both environmental and genetic factors as etiologic determinants for rheumatoid disease.

An understanding of the diagnostic laboratory examinations used to substantiate the diagnosis of rheumatoid disease is essential as the specificity and sensitivity of the RA latex fixation and sensitized sheep cell agglutination tests are often misleading. Eighty to ninety percent of patients with rheumatoid disease will eventually acquire a positive RA latex fixation test, but only thirty to fifty percent will do so during the first year. Numerous other diseases can give rise to a false positive response since the rheumatoid factor represents an anti-gammaglobulin. The sensitized sheep cell agglutination test is fifty percent sensitive but ninety percent specific for rheumatoid disease.

Finally, it should be emphasized that rheumatoid arthritis is a systemic disease which may affect the patient with constitutional symptoms, including fever, involvement of the cutaneous, occular, pulmonary, cardiovascular, hematopoietic, peripheral and central nervous systems. Our patient today had nerve compression difficulties, rheumatoid nodules, early Sjogrens syndrome, and osteoporosis which in part was provoked by the disease process in addition to corticosteroid medication.

Medical treatment of the patient with rheumatoid disease may be quite variable but should be individualized according to the patient's response and the extent of the disease. A logical progression of treatment is schematically represented by the following therapeutic pyramid (Figure 2).[2] The base of the pyramid represents a thorough medical evaluation, patient and family education, design of an exercise and rest program, and institution of anti-inflammatory medications. Although many anti-inflammatory drugs are available, salicylates remain the drug of choice particularly at the onset of treatment. Serum levels of 20-30 percent should be maintained for at least three weeks before the drug's effectiveness can be fairly assessed. If the patient's response to salicylates is unsatisfactory, other non-steroidal anti-inflammatory agents should be tried singularly or in combination with aspirin. Maximum recommended doses should be reached before discontinuing unless side effects are encountered. Analgesics, although possessing no anti-inflammatory activity, may supplement anti-inflammatory drugs from time to time for relief of pain.

If the patient's therapeutic response is unsatisfactory following this sequence of treatment, hydroxychloroquine (plaquenil) or gold should next be considered. A trial of hydroxychloroquine, 400 mg. per day for six to eight weeks, if effective should be continued with doses of 200-400 mg. per day. Because of ophthalmologic side effects, an eye examination including central visual fields with red light sensitivity is recommended every three months. The administration of gold carries with it the advantage of arresting the progression of the disease documented on the radiograph. Potential side effects include skin rash, bone marrow suppression, and renal abnormalities. Gold thioglucose (Solganl) has less systemic side effects than gold thiomalate (Myochrysine). Salicylates or other non-steroidal anti-inflammatory agents are often used in conjunction with gold.

Recently, penicillamine has been shown to be an effective oral agent for the treatment of rheumatoid arthritis as documented by its symptom relief and by the arresting of radiographic changes.[3] While the drug is not approved by the Food and Drug Administration for use in rheumatoid disease, it has been widely used by rheumatologists in this country and abroad. Penicillamine therapy begins with 250 mg. daily for twelve weeks increasing, if necessary, by increments of 250 mg. per day at twelve week intervals until a maximum dose of 1 gm. per day is reached. When a favorable response is noted, the drug is maintained at the lowest possible dose level. Side effects include those associated with gold therapy as well as taste abnormalities and interference of collagen cross-linking which is a potential hazard in wound healing. Patients allergic to gold often are not allergic to penicillamine.

If at this point in the treatment of the patient therapy has proven ineffective, one must consider the use of more toxic agents or surgical intervention. The use of corticosteroids, even at this juncture, is almost never indicated. Well-documented studies have shown that steroid therapy fails to arrest the progression of rheumatoid arthritis and carries with it significant side effects and in some instances death.[4] Patients on long-term steroids if withdrawn from the drug should be tempered gradually by reduction of 1 mg. increments per month after the administration of other anti-inflammatory treatment is begun. Alternate day steroid treatment is usually of no value. Steroid induced osteoporosis may be minimized by the addition of 1 gm. of calcium daily and 50,000 units of Vitamin D two times a week.[5]

In summary, the therapeutic treatment of rheumatoid thritis commences with salicylates and progresses in a gical and sequential fashion through the employment of gents of increasing toxicity and side effects.

urgical Treatment

obert G. Volz, M.D.

The question of surgical intervention in the patient with eumatoid disease should be considered only when edical treatment has proven inadequate. This, however, oes not exclude the orthopedic surgeon's consultation or articipation in the patient's care prior to this event as rotective splinting, bracing and exercise programs can ften be effectively guided by him. Synovectomy is dicated when recurrent joint effusions become refrac- ry to medication and their continued presence pro- okes pain, deformity, and the threat of ligamentous or ndonous damage. The knee, wrist, elbow, and meta- rpophalangeal joints are most ideally suited to syno- ectomy. The results of synovectomy in most patients, owever, are merely palliative, providing symptomatic lief for three to four or more years before recurrence of novial activity is observed. If the roentgenographic amination discloses a significant loss of the articular rtilage or joint malalignment, synovectomy by itself ill not prove effective. Osteotomy to correct an angular eformity generally has no role in the patient with eumatoid arthritis due to the commonly observed iffuse articular cartilage loss.

When significant articular cartilage loss can be demon- rated, which in the lower extremity is aided by weight- earing films, or when subchondral cyst formation or int subluxation is present, other types of arthroplasty ould be considered. These include fascial arthroplasty hich has a particular application at the elbow but should ot be used in weight-bearing joints, arthrodesis (gener- lly not practical at the elbow or knee), and total joint placement. Experiences with total joint replacement egan at the hip and now extend beyond sixteen years ith little increase in identifiable problems with con- nued usage. The current refined techniques of cemen- ble artificial joint replacement combining plastic and etal components offers the patient the greatest degree of lief of pain with the greatest potential for increased ost-operative function. Because of the dramatic clinical uccesses observed with total hip replacement, the evelopment of other types of total joint replacement llowed. Prostheses are now available for knees, ankles, oulders, elbows, wrists and joints. Although some types f prosthetic replacement should still be considered in an vestigative stage, the predictable and known post- perative results are being documented in increasing umbers in the medical literature. The overall success rate r this type of surgery ranges from 85-95 percent.

The most commonly observed postoperative problems nd complications of total joint replacement include osening of the component part, infection, and throm- oembolic disease. Although this type of surgery offers he patient the potential for dramatic relief of disability, he indications for these procedures should be closely dhered to.

Roentgenographic Examination

Michael J. Pitt, M.D.

Roentgen examination is an integral part of the evaluation of patients with rheumatoid arthritis. However, there are misconceptions regarding the contribution of this technique and the role of the radiologists in the overall assessment of the disease. The initial diagnosis of rheumatoid arthritis should be established by the primary care physician. If abnormal roentgen changes are present, the findings should support the clinical impression. Roentgenographic findings which are atypical for rheumatoid arthritis should direct diagnostic consideration towards other syndromes, i.e., other connective tissue disorders, calcium pyrophosphate deposition disease (pseudogout), and less common syndromes such as primary amyloidosis.

Complications of rheumatoid disease such as septic arthritis, secondary amyloidosis, generalized deossification, and problems related to total joint replacement may first be detected by the radiologic examination. Roentgen changes may also reflect the systemic nature of rheumatoid disease, particularly abnormalities which occur in the lung parenchyma, pleura and pericardium.

What roentgen abnormalities suggest the diagnosis of rheumatoid disease? The key to diagnosis lies in the distribution of these abnormalities as rheumatóid arthritis primarily affects joints of the appendicular skeleton. The appendicular skeletal involvement is usually symmetric and includes widening or diffuse narrowing of the joint space, changes in the subchondral cortical bone including errosions, subarticular lytic areas, deossification or new bone formation, periarticular swelling or atrophy, and joint malalignment. In the hand, involvement predominates in the metacarpophalangeal and proximal interphalangeal joints. The carpus is frequently affected and, as in other connective tissues diseases, all osseous components tend to be involved. Of consider importance is the errosive involvement of the styloid process of the ulna. The feet are also frequently involved with localization of abnormalities similar to that observed in the hand. The symmetrical involvement of joints, including the pattern of deossification and joint narrowing, is characteristic of knees, hips, shoulders and elbows.

When the axial skeleton is involved, the verbebral spine, particularly the odontoid process and the apophyseal joints, is the main target area. The sacro-iliac joints may be involved but the findings at this location are generally not prominent.

Staging of the disease by roentgenographic findings is also possible. Stage 1 is characterized by periarticular soft tissue swelling, early diffuse deossification, and often joint space widening. Stage 2 is represented by periarticular soft tissue swelling, joint space narrowing, and continued diffuse deossification. Stage 3 includes angular deformities, continued joint space narrowing, subchondral bone resorption and errosion, and progressive deossification. Finally, in Stage 4, there is complete destruction to the joint space often with bony or fibrous ankylosis, subchondral cystic change and angular deformity. (*To be continued*)

Seminars in Endocrinology and Metabolism

Occult Hypothyroidism in a Nursing Home Population

Steven M. Gonzalez, M.D.
Helen Sullivan, R.N., F.N.P.

Editors:
Stephen E. Dippe, M.D.
Jerome Targovnik, M.D.

In an elderly population the signs and symptoms of hypothyroidism are often subtle and masked by the aging process. Characteristic signs of hypothyroidism such as mental and physical slowing, dryness of the skin, hair loss, weight loss and memory impairment are often ascribed to the aging process in an elderly population. Individuals demonstrating such changes are often placed in nursing homes as they lose their capacity to care for their daily needs.

We undertook the task of screening 125 consecutive patients in five South Phoenix nursing homes for thyroid disease in an attempt to determine the frequency of occult hypothyroidism in such a population. Our results are reported herein.

Materials and Methods

As employees of the Maricopa County Health Department, we were responsible for the medical care of 270 patients within five South Phoenix nursing homes. These patients were all indigent and often were transferred with little or no accompanying information. Routine thyroid screening tests had not been previously performed on this population. The average age of these patients was 75 years with a range of 49 to 95 years. There were equal numbers of males and females.

We performed a routine thyroid function test on all new patients entering the nursing homes and on all continuing patients who became due for their annual physicial exams within a six-month period of time.

All patients were screened with a serum E.T.R. (Res-O-Mat. E.T.R.,® Mallinckrodt Nuclear, St. Louis, Missouri).[1] A normal ratio is between 0.88 and 1.13. Those patients with a ratio of less than 0.90 were screened with a TSH (Diagnostic Products, Los Angeles, California). TSH values greater than 10 U/ml were considered indicative of hypothyroidism.

Results

125 patients were screened. 80 were female and 45 were males. The preponderance of females in the study population was due to a preponderance of new female

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Dr. Gonzalez is a National Health Service Corps assignee at the South Phoenix Primary Care Center Field Site.

Address reprint requests to Helen Sullivan, South Phoenix Primary Care Center, 4732 S. Central Avenue, Phoenix, AZ 85040.

TABLE I

Case #	Patient	Sex	Age	E.T.R.	TSH (U/ml)	Response to Therapy	Months of Therapy
1.	H.R.	F	85	.77	45.4	None	1
2.	M.H.	F	67	.88	24.1	Improved	6
3.	S.P.	M	54	.85	10.6	None	5
4.	W.K.	M	68	.85	56.3	None	1

admissions during the study period.

Four patients were found to have an E.T.R. less than 0.90. All four had TSH greater than 10 U/ml, accounting for an incidence of hypothyroidism of three percent. No patient was found to have an E.T.R. in excess of 1.13. The patients' courses and values are summarized in Table I and in the following case histories.

Case 1: H.R. was a 60-year-old female who was transferred to our care in April, 1978 with the following diagnoses: schizophrenia, seizure disorder, urinary incontinence, S/P basal cell carcinoma, and "memory lapses." No other information was available. Physical exam was unremarkable except for poor intellectual function and diffusely depressed deep tendon reflexes. The E.T.R. and TSH were .77 and 45.4 U/ml, respectively. Treatment with levothyroxine, 0.05 mg/day with increments to 1.5 mg/day over the next six weeks resulted in no observable clinical response.

Case 2: M.H. was a 67-year-old female with an eight-year history of "involutional psychosis." She was treated with chloral hydrate, thioridazine and thiothixene in increasing doses without response. She became increasingly lethargic with refusal to eat. In October, 1977 examination revealed a profoundly bradykinesic female with generalized depression of intellectual function. The E.T.R. and TSH were 0.88 and 24.1 U/ml, respectively. Treatment with increasing doses of levothyroxine resulted in normalization of the thyroid function tests and a remarkable improvement in clinical status. She was taken off all psychotropic medications and was able to care for her personal needs in the nursing home.

Case 3: S.P. was a 54-year-old male who had been institutionalized in various mental facilities for mental retardation since 1939. His other diagnoses included rheumatoid arthritis and a seizure disorder. His medications included thioridazine, phenytoin and promazine. In December, 1977, examination was unrevealing except for depression of intellectual function and marked joint deformities. The E.T.R. and TSH were .85 and 10.6 U/ml respectively. Treatment with levothyroxine resulted in no clinical improvement.

Case 4: W.K was a 68-year-old male who had been chronically institutionalized with a diagnosis of "involutional depressive reaction." His medications included amitriptyline, fluphenazine, thioridazine and methylphenidate. Routine examination in May, 1978 revealed a cachetic, contracted individual who was non-communicative. The E.T.R. and TSH were .85 and 56.3 respectively. A trial of levothyroxine resulted in no obvious clinical improvement. However, the patient died approximately one month after initiation of treatment from carcinoma of the colon.

Comment

Routine screening of geriatric patients for thyroid disease has revealed that between 2.3 and 5 percent of all such patients suffered from previously clinically undiagnosed hypothyroidism.[2,3] The present study is in keeping with these results and re-emphasizes the need to do routine thyroid function studies in elderly patients.

Current thyroid assays are available in kit form and are readily performed in most community laboratories with a high degree of accuracy. Thus, screening of large populations at risk is within the capabilities of most laboratories.

The classic presentation of myxedema, weight gain, change of voice and rapid decline of physical and mental function is more often seen in the younger patient who has undergone ablation or autoimmune destruction of the thyroid gland. Common presentation in the elderly include reversible dementia, confusional states with paranoid features, syncope, ataxia, seizures, carpal tunnel syndrome, diffuse muscle pain and diminished tendon reflexes.[3] Weight is more commonly lost than gained in such patients. Hypothermia can be profound while constipation is of relatively little significance.[3]

In the case histories described above, one wonders if the symptoms of gradual intellectual impairment were the first indications of hypothyroidism rather than of mental retardation or other psychiatric maladies. Certainly early thyroid function screening would have been well warranted.

Although no statistical analysis was done, it was our general impression that there were no signs or symptoms which clearly set the hypothyroid patients apart from the 121 euthyroid patients.

It was disappointing that only one patient had a clear cut response. However, one patient had a minimally elevated TSH and the other two patients had treatment courses of less than six weeks. Indeed, the responding patient did not show signs of improvement until the third month of treatment.

Treatment should be with levothyroxine, starting at 0.05 mg per day with increments of 0.05 mg every two weeks to a maximum of 1.5 or 2.0 mg per day.

In summary, we propose that as hypothyroidism is generally occult and remarkably common in a nursing home population, all patients within such a setting undergo routine thyroid screening.

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Seminars in
Gastroenterology
and Liver Disease

Presurgical Evaluation of Patients With Recurrent or Chronic Pancreatitis

George E. Burdick, M.D.

Editors:
Leon Rigberg, M.D.
Stephen Glouberman, M.D.
George Burdick, M.D.

Management of patients with recurrent or chronic pancreatitis continues to be a difficult problem for physicians. Prior to the availability of newer techniques, particularly Endoscopic Retrograde Cholangiopancreatography (ERCP), surgical management of patients with pancreatitis was determined at exploration. Preoperative planning was seldom possible.

This paper will attempt to discuss our present approach to patients with pancreatitis who might benefit from surgical therapy.

The most common cause of recurrent pancreatitis which is surgically correctable is biliary tract disease. An oral cholecystogram is the major study to be performed in these patients. Other diagnostic studies are not necessary unless the relationship of the patient's cholelithiasis to the patient's episodes of pancreatitis is unclear. It is those patients who do not have clear-cut biliary tract disease, who may or may not be alcoholic, in which the question of surgical intervention is uncertain. A number of factors used in the evaluation of patients for surgery will be discussed below.

ETIOLOGY OF PANCREATITIS

The most common, correctable cause of pancreatitis is cholelithiasis. An oral cholecystogram is mandatory in evaluating any patient with pancreatitis even if alcoholism plays a major role in the clinical picture.

Prior to better methods of outlining the bilary tract, nonalcoholic patients were often subjected to exploratory surgery to exclude surgically correctable disease. We can now be more selective in our approach with current diagnostic studies. When the patient presents with recurrent attacks of pancreatitis, a careful search for correctable lesions includes a consideration of the differential diagnosis of pancreatitis. A partial list appears below:

TABLE 1

1. Alcoholism
2. Choledocholithiasis
3. Trauma
4. Hyperlipidemia
5. Hypercalcemia
6. Medications
7. Carcinoma Pancreas
8. Benign pancreatic tumors and cysts
9. Hereditary factors
10. Viral infections
11. Diabetes mellitus
12. Metabolic acidosis
13. Collagen vascular disease
14. Peptic ulcer disease
15. Obstruction of afferent loop (Bilroth II)
16. Pregnancy
17. Papillary stenosis
18. Side to side choledochoduodenostomy

From: 1010 E. McDowell Rd., #204, Phoenix, Arizona 85006.

PRESENCE OR ABSENCE OF ALCOHOLISM

Even the alcoholic patient may be a candidate for pancreatic surgery. The most frequent reason for surgery would be the drainage of a pancreatic pseudocyst. The timing of the surgical procedure is frequently important as the unstable alcoholic with associated liver disease is a poor surgical candidate. If a surgically approachable pancreatic lesion seems likely, the patient should be stabilized preferably for several weeks. An ERCP may then be performed and a decision made whether surgical intervention is necessary and the type of operation to be performed.

Any procedure which might leave the patient diabetic is best avoided in the alcoholic. The unreliability of most alcoholic patients can be expected to seriously complicate their diabetic management.

SEVERITY AND FREQUENCY OF ATTACKS

The frequency and severity of attacks is an obvious factor which needs to be considered before submitting a patient to pancreatic surgery. Fortunately, we usually have a preoperative diagnosis and know prior to the operation the procedure to be performed. The relative value of surgery can be weighed against the patient's clinical status before an incision is made.

ENDOCRINE STATUS OF THE PATIENT

As noted above, a major factor in determining what procedure is likely to benefit the patient is whether or not he is presently an insulin dependent diabetic. Particularly with the preoperative planning offered by ERCP, we can usually tell beforehand the procedure most likely to help the patient. Only rarely would an operation likely to produce diabetes be recommended for a benign condition.

EXOCRINE STATUS OF THE PATIENT

The presence or absence of steattorhea is not as an important consideration as diabetes mellitus, but should be considered. Steattorhea occurs relatively late in chronic pancreatitis. It does not usually occur following pancreatic surgery unless a total or near total pancreatectomy is performed. Since total pancreatectomy is only considered for very severe chronic pancreatitis or for malignant disease, the presence or absence of steattorhea seldom is a critical factor in determining management.

PREVIOUS UPPER ABDOMINAL SURGERY

The factor of prior upper abdominal surgeries will influence both the diagnostic evaluation and ease of surgical therapy.

For example, the commonly used Bilroth II procedure for peptic ulcer disease may be complicated by a marginal ulcer or afferent loop syndrome. These syndromes may present with a clinical picture simulating primary pancreatic disease. Marginal ulcers are often very difficult to diagnose with conventional radiography. However, a careful endoscopic examination, with or without a pancreatic duct study, will make this diagnosis clear.

Side to side choledochoduodenostomy is another operation sometimes followed by recurrent pancreatitis and/or cholangitis. This occurs when food particles enter the common duct through the anastomosis and become lodged in the intrapancreatic portion of the bile duct. The author has seen several patients with this problem and they have all responded well to bile duct diversion.

DUCTAL PATHOLOGY (ERCP)

The anatomy of the pancreatic duct determined by preoperative ERCP or intraoperative ductal studies is a major factor which influences the operation to be performed. A list of commonly used operative procedures appears below:

TABLE II
SURGICAL PROCEDURES IN CHRONIC OR RECURRENT PANCREATITIS

1. Cholecystectomy and/or common duct exploration
2. Sphincteroplasty
3. Side to side pancreaticojejunostomy (Peustow)
4. Distal pancreatectomy
5. Distal pancreatectomy with end to end Roux-en-Y jejunostomy
6. Subtotal pancreatectomy
7. Total pancreatectomy
8. Pancreatoduodenectomy

Pseudocysts which are demonstrated by ERCP or other procedures respond well to internal drainage of the cyst. Preoperative ERCP demonstrating the anatomy of the remainder of the duct allows the surgeon to determine if other procedures to provide ductal drainage are also necessary.

If ERCP demonstrates obstruction of one or more areas of the duct with proximal dilatation, this abnormality is best treated by a procedure offering drainage of the obstructed duct.

Additionally, preoperative ERCP will demonstrate the patient most likely to be helped by subtotal or total pancreatectomy. A decision can then be made whether or not surgical intervention should be considered based upon facts such as diabetic status, alcoholism, etc.

Hopefully, when these questions are answered preoperatively, surgical explorations of the pancreas usually ending with cholecystectomy and sphincteroplasty can be minimized. Sphincteroplasty can then be reserved for patients with true papillary stenosis.

SPECIAL STUDIES IN THE EVALUATION OF RECURRENT PANCREATITIS

Particularly useful in the evaluation of patients with recurrent pancreatitis are the following studies:

1. Abdominal ultrasound - a noninvasive, extremely valuable screening technique. Ultrasonography usually demonstrates cysts or tumors. However, confirmatory ERCP is recommended before surgical therapy is undertaken since false positives are not infrequent.
2. Computerized Axial Tomography (CAT Scan) - Although disappointing in the abdomen compared to

the success of CAT Scans of the brain, the procedure can be useful. Particularly when ultrasound is not technically feasible or ERCP is impossible or contraindicated, the CAT Scan may be the only method of obtaining adequate information regarding pancreatic anatomy.

The major disadvantages of CAT Scanning are:

a. Expense

b. The fact that the information is not reliable enough to be used as the sole source of information prior to surgery. Confirmatory ERCP is almost always indicated, if possible.

3. Endoscopic Retrograde Cholangiopancreatography (ERCP) - The most valuable study in evaluating possible surgical disease of the pancreas. ERCP provides excellent detail of ductal anatomy. Decisions can usually be made as to whether surgery is feasible and what type of surgery should be performed. The major disadvantage of the procedure is the availability of physicians with experience with the technique as well as experience in interpretation of films.

WORKUP OF PATIENTS WITH CHRONIC OR RECURRENT PANCREATITIS

1. History and physical examination
    a. Alcoholism
    b. Trauma
    c. Family history
    d. Medications
    e. Surgery
2. Oral cholecystogram
3. Liver profile
4. Fasting and two-hour post prandial blood sugar
5. Lipid profile
6. Serum calcium
7. Upper GI series
8. Careful review of medications
9. Ultrasound
10. ERCP (If surgical therapy is contemplated)
11. CAT Scan - (Because of expense, my personal preference is to reserve CAT Scanning for those patients where ultrasound is not technically adequate or the patient is too ill to have ERCP. The CAT Scan is rarely good enough to be the only source of preoperative information.)

Additional studies occasionally useful in the evaluation of recurrent pancreatitis include:

1. Intravenous or percutaneous transhepatic cholangiogram
2. Biliary drainage
3. Arteriography
4. Secretin test
5. Three-day stool fat

SUMMARY

With present day technology, a great deal of information can be learned about patients with chronic or recurrent pancreatitis prior to surgery. With this knowledge, a decision can be made as to whether the patient needs surgery and what procedure is most likely to be helpful.

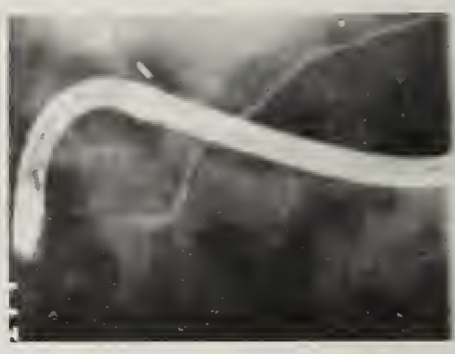

FIGURE 1

FIGURE 2

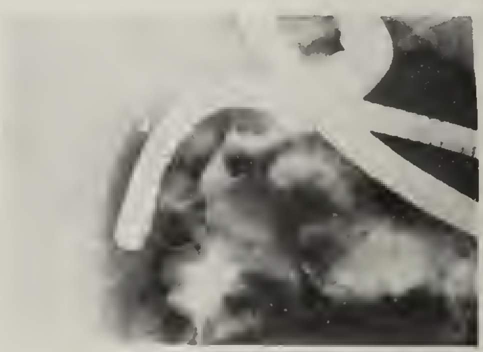

FIGURE 3

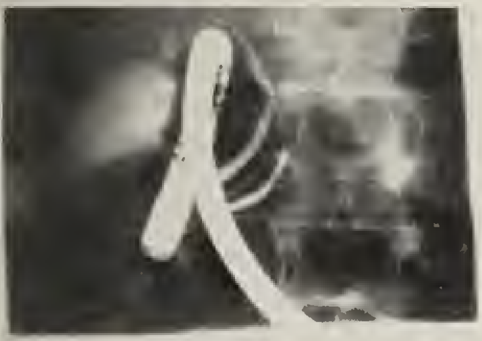

FIGURE 4

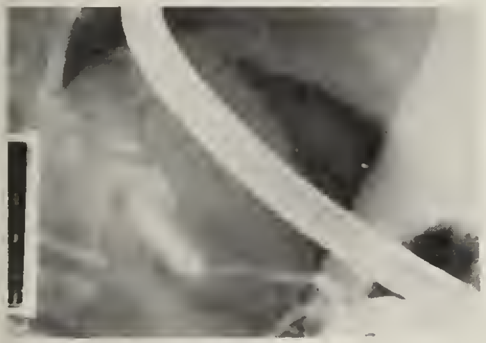

FIGURE 5

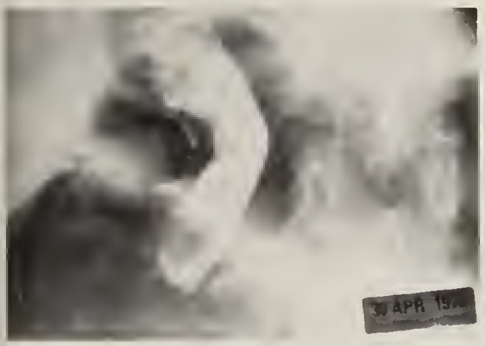

FIGURE 6

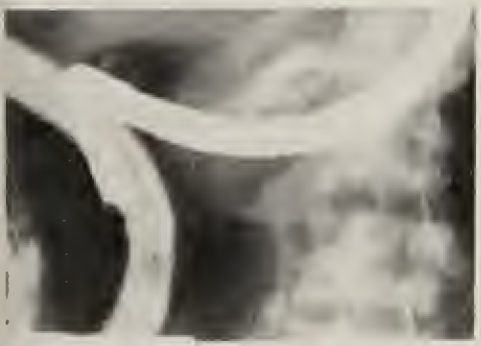

FIGURE 7

LEGENDS

1. Normal pancreatic duct. This does not exclude chronic pancreatitis.
2. Irregular, beaded, pancreatic duct in a non-diabetic alcoholic Recommendation - no surgery. Would probably require subtotal or total pancreatectomy for pain relief.
3. Common duct stones causing recurrent pancreatitis.
   Recommendation - Exploration of common duct with removal of stones.
4. Normal common bile duct and gallbladder. Obstruction of pancreatic duct due to cancer.
   Recommendation - Surgery as appropriate for stage of tumor.
5. Pseudocyst in post cholecystectomy patient. Pancreatitis secondary to stones.
   Recommendation - Cyst-gastrostomy. Common duct exploration with removal of residual stones.
6. Food particles in common duct. Patient with side to side choledochoduodenostomy with recurrent pancreatitis. Endoscope has been removed.
   Recommendation — Choledochojejunostomy (Roux-en-y).
7. Dilated pancreatic duct in alcoholic pancreatitis - nondiabetic. Recommendation — Side to side pancreaticojejunostomy (Peustow) or distal pancreatectomy with Roux-en-Y jejunal loop.

Infectious Disease

Mixed Anaerobic Infections

Part I

Barry A. Friedman, M.D.

In the last several years we have begun to recognize the importance of mixed anaerobic and aerobic infections. What follows is a review of the microbiologic, diagnostic, and clinical features of these serious infections, which hopefully will serve as a guideline in evaluating and treating such patients.

Microbiology

Anaerobic bacteria are those bacteria which cannot grow in the presence of oxygen. These organisms are Gram positive or negative and may be either rods or cocci. Unlike the "usual" aerobes, anaerobic bacteria require an atmosphere free from oxygen, a medium which has a lowered redox potential, and growth factors similar to those found in necrotic debris. Previously available in only the most sophisticated research laboratory, these conditions are reproducible today in any laboratory using commercially available material. Representatives of this class of bacteria include: Bacteroides (fragilis and species), Fusobacterium, Anerobic streptococci, Veillonella, Clostridia, and Eubacterium. Many of these bacteria produce gas and have foul odor and they generally grow more slowly than anaerobic organisms.

Anatomic Considerations

In man, the normal milieu which will support the growth of anaerobes (plus aerobes) is present in three major anatomic sites: oropharynx (especially in the dental crypts) female genitourinary tract and the lower gastrointestinal tract including the colon and distal ileum. In health, within each region, microbiologic relationships are almost always the same within an individual and are essentially the same from person to person. (Table 1).

TABLE I
NORMAL ANEROBIC BACTERIAL DISTRIBUTION IN MAN

	Bacterial Distribution		
	Colon	**Genitourinary**	**Oropharynx**
Anaerobes	Bacteroides fragilis	Peptococcus	Bacteroides fragilis
	Clostridia	Peptostreptococcus	B. Melaninogenicus
	anaerobic cocci	Bacteroides fragilis	Fusobacteria
		Clostridia	Peptostreptococcus
			Eubacterium

Numerically, colonic anaerobes, composed primarily of Bacteroides fragilis, outnumber the most common aerobe (E. Coli) 1000:1. In the female GU tract, anaerobes again outnumber aerobes. Here the primary anaerobes are peptococci and bacteroides. Unlike the GI and GU tracts, the oropharynx is colonized by smaller numbers of anaerobes but usually has more cocci than either of the other two sites.

In health, these relationships generally persist. More importantly, *in illness, these same bacteria are found outside their normal milieu and in approximately the same numerical ratios as found in the area from which they came.* For example, in a subphrenic abscess following repair of a gunshot wound to the colon, the bacteria found in the abscess should be those typically found in the colon. This will be true even when the

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From: 5629 E. Grant Rd., Tucson, AZ 85712.

picture has been altered somewhat by antecedent surgery and the use of antibiotics.

Clinical Considerations

Anaerobic infections usually present with symptoms similar to those of other infectious processes. They can also mimic non-infectious illness. For example, a brain abscess might present with any combination of headache, focal findings, seizures, or increased intracranial pressure. The patient with an intraabdominal catastrophe may complain only of abdominal pain, nausea and vomiting. The post partum patient may complain of pelvic pain and cramping. Post-operatively, a wound infection may be easily recognized by the surgeon.

There are however certain findings which strongly suggest the involvement of anaerobes in the infectious process. (Table 2).

TABLE 2
KEY FEATURES OF ANEROBIC INFECTIONS

1. Foul odor in the involved area
2. Gas production
3. Necrotic debris associated with purulent material
4. Disruption of the integrity of the mucosa of the oropharynx, GI or GU regions with adjacent infection.
5. The occurrence of infection in an area frequently associated with anaerobes
   a. GI- ruptured diverticuli, appendiceal abscess
   b. GU- tubo ovarian abscess, endometritis
   c. Oropharynx- brain abscess, aspiration pneumonia

Once the presumptive diagnosis and the location of the anaerobic infection have been established, the next clinical maneuver is proper culturing. Aerobic cultures may be obtained in the "usual" fashion, using a transport medium, taking care not to send the laboratory a dry swab. A more ideal method of collection is aspiration of purulent material into a glass syringe. All air is removed from the syringe which is then capped and sent immediately to the laboratory where not only aerobes can be cultured, but anaerobes as well. Anaerobic organisms can also be transported in special containers. Care again must be taken to insure that an anaerobic atmosphere be maintained during collection and transportation of the specimen. This specimen also should be transported immediately after collection.

Summary

In summary, mixed anaerobic infections are usually caused by both aerobic and anaerobic bacteria which are harbored in three major anatomic regions. Disruption of the integrity of one of these regions leads to adjacent or metastatic infection. These infections usually have a predictable bacterial flora which is similar to that found in the site of origin of the infection process.

Treatment of these infections usually involves aggressive surgical debridement and drainage accompanied by appropriate antibiotic therapy. (*To be continued.*)

Burn Toxins and Supression Of the Immune Response

Stanley J. Archer, Ph.D.
Sharli L. Herrington, B.S.
Maj. Virginia L. Rodriguez, B.S.

An attempt has been made to correlate the formation of toxic substances in the skin following severe burns and the suppression of the immune response which occurs in burn victims. In the course of this investigation, "burn toxin" was prepared from burned mouse skin which severely suppressed the immune response. Apparently, the active immunosuppressive components of the toxin are cytotoxic for lymphocytes and thus mediate suppression of the immune response. The possibility of abrogating the immunosuppressive activity of the burn toxin by passive immunization is discussed.

From: Department of Botany-Microbiology, Arizona State University, Tempe, AZ 85281. (Dr. Archer & Ms. Herrington). Reprint requests to Dr. Archer. USAF Aerospace Medical School, Brooks AFB, TX 78235. (Maj. Rodriguez).

BURN TOXINS AND SUPPRESSION OF THE IMMUNE RESPONSE

In recent years, progress in burn therapy has virtually eliminated death resulting from primary shock and early infection following severe burns. In contrast, statistics reveal that in the last decade there has been no significant decrease in the mortality rate after full-thickness burns involving 55% or more of the body surface.[1] Thus, the emphasis in burn research has shifted to the problem of "late mortality." Also, interest has recently increased in the possibility that one or more toxic substances are produced in the skin by thermal energy during severe burns and that these substances are responsible for late "burn diseases."

Indeed, toxic substances formed from burned skin have been reported in a number of cases. Most of these reports have dealt with a high molecular weight lipoprotein extracted from burned mouse skin.[2-6] This lipoprotein is apparently formed by polymerization of structural membrane components following thermal injuries. A burn toxin, which is lethal when injected into mice, has also reportedly been extracted from burned human skin. Furthermore, the lethal activity of the toxic material can be neutralized by passive immunization with anti-burn toxin antiserum prepared in rabbits.

Clearly, burns involve much more than simply the loss of skin and exposure of the underlying tissues to bacterial infections, since many pathophysiological complications are known to occur following severe burns. One complication which accompanies severe burns is the critical impairment of immune responses, particularly cell mediated immune responses.[8-10] Evidence for such an impairment is the prolongation of skin graft survival time, a decrease in the delayed hypersensitivity response, a diminished graft versus host response, and a decreased mitogenic response of lymphocytes from burn patients.

Recently, we have attempted to establish the relationship between burn toxins and suppression of the immune response using a burn toxin extracted from mouse skins. Briefly, to prepare the burn toxin, mice were killed by cervical dislocation, the skins removed, shaved, and the subcutaneous fat removed. The mouse skins were then pressed against a metal surface heated to 250°C for 25 seconds. This burn resulted in approximately 40% weight loss of the skin. The extraction procedure described by Schoenenberger *et al.*[1] was then used to prepare the toxin.

Intraperitoneal injections of sublethal doses of the burn toxin in mice were found to suppress the primary immune response to a concomitant antigenic challenge with sheep erythrocytes as measured by the Jerne hemolytic plaque assay. In subsequent experiments, the crude burn toxin was fractionated by sephadex gel filtration into high and low molecular weight fractions. Portions of each fraction were then injected into mice which were challenged with antigen. It was found that the high molecular weight fraction of the burn toxin completely suppressed the immune response while the low molecular weight fraction had no effect on the immune response.

To investigate the mechanism by which the burn toxin mediates suppression of the immune response, the toxin was added to mouse spleen lymphocytes in culture. By monitoring the vaibility of the lymphocytes at different times following addition of the toxin, it was found that the toxin caused a rapid decrease in lymphocyte viability. Similar extracts prepared from unburned mouse skin had no effect on lymphocyte viability.

By comparing the extracts prepared from unburned and burned mouse skins, we were able to evaluate chemical changes which occurred following application of thermal energy. Using sodium dodecyl sulfate polyacrylamide gel electrophoresis and Ouchterlony double immunodiffusion, we found that not only are new antigenic determinants formed following a burn, but numerous components appear which are not present in normal skin. It is apparently one or more of these new components which suppress the immune response.

Work is now continuing in an attempt to identify the component(s) which are toxic to lymphocytes and mediate suppression of the immune response. When this is accomplished, antiserum will be made to the component(s) and an attempt will be made to abrogate the immunosuppressive effect of the toxin by passive immunization.

It is anticipated that this line of investigation will lead to a better understanding of the suppression of the immune response which follows severe burns in humans. It is also hoped that this study will provide insight into how the victims of such burns may be treated so as to provide an increased chance of survival.

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Obstetrics and Gynecology

Emergencies in the Delivery Room (Part II)

John V. Kelly, M.D.

Donald J. Ziehm, M.D., Editor

POST-PARTUM HEMORRHAGE

"Be prepared" — a good maxim for boy scout and obstetrician alike. The patient with twins, polyhydramnios or a little giant, and the lady whose labor lasted 24-48 hours and/or required oxytocin for her "lazy womb" — all are good candidates for uterine atony. The use of an oxytocic immediately after delivery of the placenta promotes rapid uterine contractions and is excellent prophylaxis against uterine atony. It is prudent to remember that oxytocin should be given in an infusion (10-20 units/liter) rather than as a bolus of 5-10 units IV since the latter can cause acute hypotension, myocardial arrhythmias, cardiac arrest and death. Ergot preparations have a tendency to cause vasoconstriction and severe hypertension in a small percentage of patients and probably should be avoided in pre-eclamptic or eclamptic patients.

Once atony occurs, three traditional maneuvers are appropriate:

1. Manual massage to provoke uterine contractions.
2. Elevation of the uterus out of the pelvis.
3. Bimanual examination to obtain marked anteversion of the uterus, as well as massage and digital compression in the paracervical areas where the uterine arteries enter the uterus.

Sometimes uterine atony persists despite treatment with drugs and massage, and no other source of bleeding can be identified. In these situations I am a strong advocate of the old method of intra-uterine packing. Packing is indeed a controversial subject, but in over 25 years of practicing obstetrics in both primitive and civilized countries, I have been convinced that pressure via a pack against the placental bleeding site saves blood loss while preparing for surgery, often makes hysterectomy unnecessary, and sometimes saves lives. The prepared material is plain gauze of 4-inch diameter and 6-ply thickness. In an emergency situation, simply tying 4 by 8 inch gauze pads together end-to-end is effective. With the fundus of the uterus in the packer's hand, the gauze is inserted with a long dressing or packing forceps and firmly positioned, starting at one corner or the other. It is essential that the upper part of the uterus be fully packed. A large amount of gauze is required; 10-15 yards of gauze should be used to tightly pack a postpartum uterus. If bleeding occurs through the packing, removing the packing and repacking the uterus is a waste of time and is dangerous.

Removal of packing from the uterus is best carried out in 24 hours with preparations arranged either for repacking or for surgery in case of recurrence of bleeding. A key to success with the management of hemorrhage from uterine atony is the use of common sense. Thus, drastic efforts to save the uterus of a multiparous woman would be foolhardy.

At times the only hope for treatment is surgery. One has 2 choices: ligation of the hypogastric (internal iliac) arteries with heavy chromic or silk sutures, or hysterectomy. In critical situations, sub-total hysterectomy may be necessary, leaving the cervix behind because of the need for speed and limitation of anesthesia.

With a patient in shock, plasma expanders, such as Ringer's Lactate are mandatory. Administration of type-specific blood is wise when a delay is expected for cross-matching. The use of vasopressors to restore blood pressure and improve cardiac output in hemorrhagic shock should always be secondary to adequate volume replacement. Their use is restricted to occasional cases in which shock prevails despite adequate fluid replacement, and renal shutdown is imminent. The sympathomimetic

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Dr. Kelly is Chairman, Department of Ob/Gyn, Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008, and Professor, Department of Ob/Gyn, University of Arizona Medical Center.

drug of choice is dopamine hydrochloride (Intropin). The intravenous dosage is 2-5 ug/kg/min. It is unlike the other drugs used in shock to elevate the blood pressure (norepinephrine, epinephrine and isoproterenol) in that it increases the blood flow to the kidneys. In addition, employment of 100% oxygen by mask, cortisone in large doses when adrenal failure is suspected, and antibiotics are all integral aspects in the management of hypovolemic shock.

Lacerations of the cervix or vagina, another cause of postpartum bleeding, are best repaired by continuous running locked suture. Deep lacerations should be closed in layers to avoid the leaving of "dead space" for hematoma accumulation. Packing of the vagina with gauze is a very helpful method for controlling venous oozing or bleeding from varicose veins. Temporary hemostatic control of cervical lacerations may be quickly achieved by applying ring forceps to the edges of the laceration. Not infrequently the cervical tissue is so edematous or friable that sutures either will not hold or may seem to aggravate more bleeding, or both. In such cases, the use of either ring or sponge-holding forceps, or packing of the cervix and vagina may be the optimal management. When ring forceps are applied, they can be left in place for several hours. The use of these techniques is also prudent when a cervical laceration has extended up into the uterus or broad ligament, requiring entry through the abdomen to achieve control of bleeding. Assistants, retractors and good light are essential for repair of lacerations.

The retained placenta can be responsible for serious postpartum hemorrhage. Manual removal is imperative; it is best achieved by finding a cleavage plane via careful digital exploration. If this cannot be determined at the lower pole of the placenta, the upper and lateral aspects should be explored. The fingers are kept together and the placenta is carefully and deliberately separated from the uterine wall. Traction on the body of the placenta prior to digital separation is unwise for it may result in its incomplete removal or in inversion of the uterus. Sometimes the placenta just cannot be removed intact, and piecemeal evacuation is necessary. Should this become necessary, one must be careful to not dig into the uterine wall; perforation, particularly of the thinned lower segment, may ensue. Removal of the placenta is occasionally difficult, even under direct vision at cesarean section. At these times, small fragments may not be able to be removed and must be left in situ. Completion of the removal is often achieved by use of gauze over the gloved hand to provide "friction curettage" of the placental site. A large, dull curette may also be used to extract any residual placental tissue.

When placenta accreta is suspected because of inability to separate the placenta, one should desist from further efforts at removal and make immediate preparations for laparatomy. If uterine bleeding is a problem in such cases, packing of the uterus is a very helpful temporary measure until the abdomen can be opened and hysterectomy performed.

Oncology

Bladder Cancer:

Current Status of Diagnosis & Treatment

Thomas H. Stanisic, M.D.

Editor:
David Alberts, M.D.

INTRODUCTION

Bladder cancer is the eleventh leading cause of cancer death in the United States today and kills approximately 9,000 Americans annually.[1] It is three times as common in men as in women. Most bladder tumors are of transitional cell origin, although squamous cell carcinomas and adenocarcinomas are not uncommon. Although it is virtually impossible to identify specific responsible carcinogenic agents in the individual patient, epidemiologic and laboratory studies indicate that certain environmental factors are associated with an increased risk of contracting bladder tumors. Exposure to aromatic amines, as in the dye industry, schistosomiasis, and cigarette smoking are well-established "high-risk" factors. However, the evidence linking cyclamate or nitrite ingestion, abnormal tryptophan metabolism, pelvic irradiation, and analgesic abuse with bladder neoplasia is less firm.[2]

Classically, gross, total painless hematuria is the most common presenting symptom, but many bladder tumor victims initially present with unexplained irritative symptoms (urinary frequency or dysuria), or with microscopic hematuria on routine urinalysis. Any patient presenting with one or more of these signs or symptoms should be intensively and thoroughly evaluated with the diagnosis of bladder tumor in mind. Cystoscopy by a competent urologist, with biopsy of suspicious or obviously abnormal bladder mucosal lesions, is, of course, essential to any adequate evaluation. Intravenous urography is a useful adjunct, but most bladder tumors are too small to be visualized on routine studies. Urinary cytology is helpful but is associated with 5 percent to 15 percent false positive rates in most series, while false negative results may be as high as 30 percent, especially

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From: University of Arizona Health Sciences Center, Tucson, AZ 85724, Thomas H. Stanisic, M.D., Assistant Professor of Surgery/Urology.

when low-grade lesions are considered.[3] However, ytology may be extremely helpful in detecting the presence of unsuspected carcinoma *in situ*.

NATURAL HISTORY

Prognosis in any particular bladder cancer depends upon the *grade, stage*, and *multicentricity* of the tumor.

Grade refers to the degree of tumor anaplasia as demonstrated on histopathologic sections and takes into account cell size and nuclear variations, mitotic activity, etc. Tumors are generally graded on a I-IV basis with grade IV lesions being the most anaplastic and associated with the worst prognosis.

Tumor *stage* refers to the depth of invasion of the umor into the bladder wall, and the presence or absence of distant metastases. The problem of clinical staging is a discussion in itself, but, basically, depth of invasion is determined by the examining urologist through careful ransurethral biopsy of the bladder tumor, bimanual examination, and intravenous pyelography. Screening for metastases is essential and includes chest X-ray, bone scan, liver function tests, and even pelvic arteriography and lymphangiography in some centers. The Jewett-Strong-Marshall[4] classification system is used by most American urologists today. In this system, stage O is assigned to papillary, non-invasive carcinoma. Stages A, B$_1$, B$_2$, and C are assigned to tumors which invade, respectively, bladder submucosa, superficial muscle, deep muscle, and full thickness of the bladder wall. Stage D$_1$ refers to tumors involving adjacent pelvic organs or pelvic lymph nodes, while stage D$_2$ tumors have metastases outside the pelvis. Low-grade tumors, in 75 percent of the cases, are associated with low stages as well. Generally, superficial tumors (stages O, A, B$_1$) are associated with a good prognosis if adequately treated locally, while deeply invasive tumors (stages B$_2$, C) have an ominous prognosis. Once metastatic (stages D$_1$, D$_2$), bladder cancer is rarely if ever curable.

The importance of the *multicentricity* of neoplastic and preneoplastic changes within the patient's bladder has only recently been recognized. Although tumor stage and grade are of undeniable importance in determining the short-term prognosis for the patient, the malignant potential of the urothelium left behind when a single tumor is removed is of great prognostic significance. Studies of total cystectomy specimens indicate that invasive bladder cancer is often associated with grossly inapparent, and often extensive, carcinoma *in situ* in seemingly normal portions of the bladder mucosa. Other studies indicate that such *in situ* changes may even presage the development of grossly invasive lesions in 50 percent to 60 percent of cases. At present there is no generally accepted or proven method of assessing the multicentricity of malignant potential within the urothelium, although the value of urinary cytologies and random bladder biopsies at the time of tumor resection is being studied intensively.

TREATMENT

Superficial tumors (stages O, A, B$_1$): Most superficial tumors can be managed in a relatively straightforward manner by transurethral resection and coagulation of the tumor base. Such treatment generally results in complete ablation of the individual tumor and is well tolerated by the patient with minimal morbidity or mortality. Occasionally, superficial tumors, by virtue of their size, location, or multiplicity, cannot be eradicated transurethrally for technical reasons and a formal open operation (usually segmental resection of the portion of the bladder) is required. Although this is a somewhat more extensive procedure than transurethral resection (1%-2% mortality), the results are comparable with regard to tumor eradication.

Unfortunately, 75 percent to 80 percent of patients initially presenting with superficial tumors will later have recurrences[5] and regular cystoscopic examinations are required for an indefinite period. Most of these recurrences occur with 5 years of the time of diagnosis of the initial tumor. Many other patients are tumor free for some time only to develop a recurrence 5-10 years later.

Some urologists screen for recurrence with cytologic examination of the urinary sediment, but I personally have encountered false negative reports all too frequently, especially with low-grade lesions and, thus, rely primarily on cystoscopic examination for follow-up. When superficial recurrences are detected, they are also treated by transurethral resection. When recurrences are frequent or numerous, periodic intravesical thiotepa instillation (60 mg in saline diluted to 100 cc) weekly for 6 weeks will diminish the number and frequency of recurrences in ⅓ to ⅔ of patients.[6] In addition, 5 percent to 10 percent of patients initially presenting with superficial bladder tumors will develop renal pelvic or ureteral neoplasms, so annual examination of the upper urinary tract by intravenous pyelography is advisable. Obviously, the patient with a typical bladder tumor gets to know his urologist quite well as he lives with his disease, and the costs to the patient in terms of dollars and time lost from work are obvious.

More ominous is the fact that 20 percent to 30 percent of individuals whose first tumor is superficial will go on to develop invasive cancer at a later date, even when they are closely followed and superficial recurrences are treated appropriately.[5] When this invasive cancer occurs, prognosis and treatment plans are radically altered. Currently, there is no way to predict with certainty which individuals will go on to develop invasive tumors and, obviously, no way to alter the biologic potential toward further malignant degeneration in such patients.

Invasive clinically localized tumors (stages B_2,C): In contrast to the general agreement on the treatment of superficial tumors, there is no unanimity of opinion among clinicians treating bladder cancer as to the optimal management of invasive lesions. All experienced clinicians will agree, however, that, at present, whatever treatment modality is utilized for invasive cancer, the results are extremely discouraging. An optimist might point out, however, that results with one mode of treatment are somewhat less discouraging than with others.

During the 1960's many institutions gained considerable experience with the treatment of invasive bladder cancer by either high-dose bladder and pelvic node irradiation or by total radical cystectomy with urinary diversion. The results, in terms of 5-year survival for clinical stage B_2 or C disease, vary among institutions but average only 15 percent to 30 percent with either modality used alone.[7] With irradiation, the major complication rate (chiefly bowel and bladder complications) is approximately 8 percent to 14 percent, while minor complications are more frequent (50%-70%). We have found the complication of radiation cystitis with chronic, recurrent, often massive bleeding to be especially devastating on a long-term basis. Radical cystectomy and urinary diversion, on the other hand, are associated with 3 percent to 10 percent perioperative mortality and a major complication rate of 20 percent to 30 percent. With irradiation failure, local recurrence in the retained bladder is common, while recurrence within the pelvis is frequent post cystectomy. Distant metastases, of course, ultimately occur with failure from either modality, unless death supervenes.

More recently, however, improved results have been reported from several large centers utilizing an integrated therapeutic approach combining preoperative bladder and pelvic irradiation (doses vary but are generally reduced), with subsequent radical cystectomy and urinary diversion. Most reports indicate that such an approach markedly improves 5-year survival rates compared with either irradiation or cystectomy alone. Reported 5-year survival with combined therapy ranges from 30 percent to 51 percent.[7,8] Surprisingly, reported morbidity and mortality of surgery are not increased, and our experience at the University of Arizona agrees with this.

Despite these encouraging improvements in results in recent years with intensive treatment of localized tumor, one must recall that the vast majority of patients with invasive bladder cancer still die of their disease with distant metastases. Presumably, distant dissemination has already occurred at the time treatment of pelvic disease has begun, and some form of effective systemic therapy is essential to further increase survival. Unfortunately, no such agent (or combination of systemic agents) is demonstrably effective in this setting at the present time.

Metastatic disease (stages D_1, D_2): Surgery offers little hope for cure of metastatic disease. A possible exception to this is the patient whose metastases are limited to organs immediately adjacent to the bladder or to the pelvic nodes distal to the iliac bifurcation. Whitmore et al report 8 percent to 14 percent 5-year survival with combined radiation therapy and cystectomy in a limited number of such patients.[8] In most cases, however, individuals with metastases must rely upon chemotherapy for palliation of their disease, and thus far the response to most chemotherapeutic agents has been discouraging. Few controlled clinical trials have been performed and most reports represent anecdotal experiences with few patients. Reported results vary greatly from institution to institution.[9] The pyrimidine antagonist 5-fluorouracil has been utilized by many workers as a single agent and reported objective response rate varies from 0-75 percent. Similarly, reported response rates to doxorubicin (Adriamycin) (5%-37%), cyclophosphamide (0-53%) and methotrexate (17%-36%) are highly variable. Reported results with *cis*-diamminedichloroplatinum are more promising (33%-47%), but the median duration of response is short (4.8 months). Currently, combination chemotherapy of advanced disease with cyclophosphamide, doxurubicin, and *cis*-platinum is being evaluated at the University of Arizona.

Local bladder symptoms, secondary to residual tumor or previous treatment, can often be alleviated by specific therapy. Simple transurethral resection of bleeding recurrent tumors is often effective. Intravesical instillation of 1 percent to 10 percent formalin will temporarily relieve chronic or massive hematuria in most patients We have treated bleeding from non-resectable tumor recurrences and from radiation cystitis with this agent. General or spinal anesthesia is required during the 15-minute instillation, and a preliminary cystogram is essential to rule out vesicoureteral reflux. If reflux is present, the ureters must be occluded with Fogarty catheters endoscopically to prevent renal damage. We use 1 percent formalin in preference to higher concentrations since reported complications are less frequent with dilute solutions.

Palliative bladder irradiation will also control hematuria on a temporary basis in many instances, but bladder pain and irritability are often worsened. Supravesical diversion of the urine is sometimes necessary, either alone or as an adjunct to any of the above measures, to aid in control of local symptoms. Of course, surgical morbidity and mortality are significant. Pain from bony metastases is often relieved by short-term radiation therapy to involved areas.

CURRENT RESEARCH AND FUTURE GOALS

Although we are certainly better able to deal with vesical neoplasms today than in years past, there have been no real therapeutic breakthroughs in recent years which markedly improve survival. Superficial tumors are treated today essentially as they were in 1950. Such lesions are locally excised, while urologist and patient together hope and pray that invasive lesions do not develop. Nevertheless, invasion does occur, inevitably, at the same 20 percent to 30 percent rate today as it did 30 years ago. Invasive lesions are better treated today by combinations of radiation therapy and surgery, but even successful therapy results in massive changes in the patient's lifestyle and body image, and the majority of individuals with invasive tumors still die of their disease. Occult systemic dissemination of disease has already occurred in many when hopefully curative treatment is initiated. Obviously, survival figures would improve if those superficial tumors with biologic potential to invade and destroy could be identified prior to invasion and singled out for earlier, more effective treatment. Three lines of current investigation give some promise of progress in this regard.

Cytogenetic analysis of the karyotype of superficial tumors indicates that those with certain "marker chromosomes" are much more likely to give rise to invasive tumors in the future. There is also evidence to indicate that such superficial tumors with "invasive potential" lose their surface A, B, H antigens long before invasive tumors appear. In addition, urinary cytology and random biopsy of grossly normal urothelium are effective in the detection of carcinoma *in situ*. Over 50 percent of such patients will later develop an invasive carcinoma, and early treatment by cystectomy when the disease is in the *in situ* phase is usually curative.

In addition to the need to further improve our ability to detect urothelial lesions with malignant potential, improved survival from bladder cancer requires the development of effective systemic chemotherapeutic agents. Most individuals with invasive disease die with distant metastases despite effective local exenterative surgery and irradiation. Presumably, effective adjuvant chemotherapy at the time of surgery would markedly improve survival by destroying occult distant microscopic metastases. At present, however, routine adjuvant therapy is felt by many to be impractical since clinical response to the presently available highly toxic agents is unpredictable in the individual case, and the risks thus outweigh potential benefit.

Recent work at the University of Arizona Cancer Center with *in vitro* tumor colony assay of ovarian cancer and multiple myeloma tumor stem cells indicates that chemotherapy can be individually tailored successfully on the basis of such "*in vitro*" sensitivity testing.[10] With slight modification, we have recently used the same cell culture system to grow bladder cancer stem cells *in vitro* in predictable fashion. Currently, evaluation of the system for *in vitro* sensitivity testing of bladder cancer to specific chemotherapeutic agents is underway. Bladder tumor tissue is easily accessible in most patients via transurethral resection and/or bladder barbitage. We have already established that tumor cells obtained in this manner do, indeed, grow in this culture system. When sufficient patient data are accumulated, we hope to make some progress toward more rational selection of drugs for treatment of advanced disease. Ultimately, such a system may make chemotherapy useful in an adjuvant setting as well.

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Psychiatric Disorders

Key Concepts in the Diagnosis and Management Of Depression for the Family Physician

Management, Part II

Thomas E. Bittker, M.D.

As a teaching convenience, I have termed the first five principles of management as the five "A's" in the treatment of depression.

I. Accessibility

The physician who treats the depressed patient should schedule frequent, brief office visits involving not only the patient, but also the patient's family. Telephone encounters, after the initial interview, can further support the patient and his family.

II. Appraisal of Pathological Assumptions

Most patients have been over-invested or have over-valued something which they now interpret as a major loss. Challenge the assumption that this loss means the end of the patient's productive life or reflects on the patient's basic worthiness. Explore alternative assumptions. Help the patient become aware of the link between these pathological assumptions; maladaptive behavior and passivity; and the consequent feelings of low self-esteem.

III. Activity

Encourage the patient to take small steps in resuming previously valued activities. In doing so, the physician is offering some hope for return to function. Small successes can serve as a foundation for rebuilding self-esteem. Patients should not anticipate experiencing pleasure in these activities immediately; many times the pleasure response is delayed; rather, these activities help the patient restore positive life-habits.

IV. Anti-Suicide Contracting

Explore with all depressed patients the possibility of suicide and their capacity to maintain self-control over these impulses. Acknowledge to the patient your awareness of the level and intensity of the suicidal impulse. Remind the patient that he probably has some mixed feelings about this impulse or otherwise he would not be seeking help. At the same time, make the patient aware that you do take the suicidal feelings seriously. Remind the patient that suicidal impulses are typically short-term and are often a product of a distorted perspective of life events and will change with time. As long as the patient is experiencing suicidal feelings, drinking alcohol or taking medication that would compromise judgment should be discouraged. Finally, obtain a specific commitment from the patient to refrain from behavior destructive of himself or others. I have found the following helpful: "No matter what happens, I would like an understanding from you that you will not do anything intentionally to hurt yourself or to hurt others. How long do you feel you can commit yourself to this agreement?" Accept whatever commitment the patient can make whether it be for a few hours or for several months. Should the patient feel that at any time he cannot honor his agreement, emphasize that you would expect him to inhibit his impulses at least until such time as you will be available for consultation. At the expiration of the above agreement, arrange to renew the agreement with the patient.

V. Antidepressants and Mood-Modifying Agents

Should the patient warrant the administration of antidepressants and mood-modifying agents, explore with him ahead of time how he feels about taking medicines. Explain to the patient that medicines provide only a partial solution to depression. Medicines will treat the chemical component. The patient, his family and his physician must work as partners in treating the cognitive and interpersonal elements contributing to depression.

Prior to the administration of antidepressants, all

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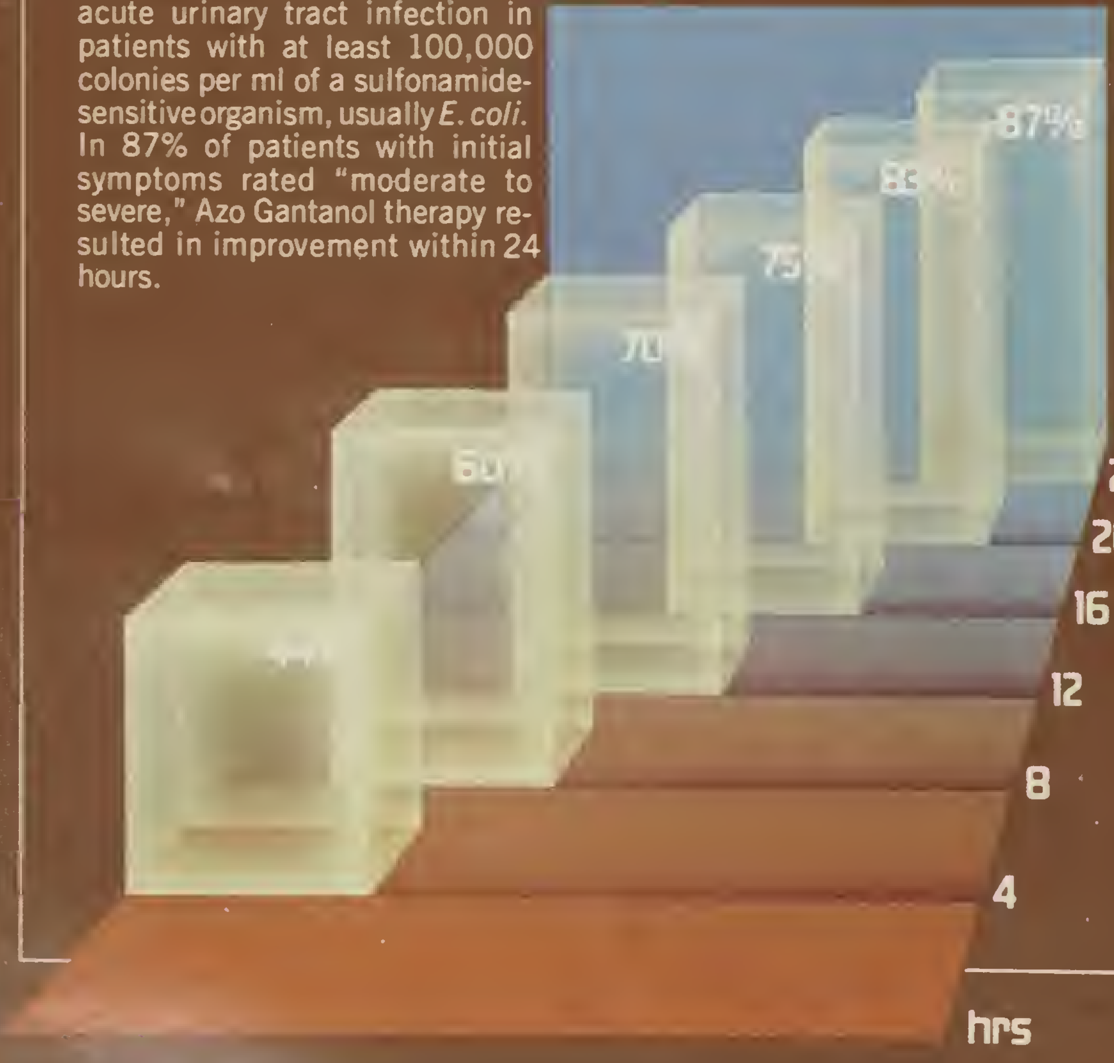

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Indications: In adults, urinary tract infectio
complicated by pain (primarily pyelonephrit
pyelitis and cystitis) due to susceptible orga
(usually *E. coli, Klebsiella-Aerobacter, Staph*
coccus aureus, Proteus mirabilis, and, less
quently, *Proteus vulgaris*) in the absence of
obstructive uropathy or foreign bodies. **Note:**
fully coordinate *in vitro* **sulfonamide sensiti**
tests with bacteriologic and clinical respons
aminobenzoic acid to follow-up culture med
increasing frequency of resistant organisms
the usefulness of antibacterials including su
fonamides. Measure sulfonamide blood level
variations may occur; 20 mg/100 ml should
maximum total level.

Contraindications: Children below age 12; s
fonamide hypersensitivity; pregnancy at ter
during nursing period; because Azo Gantano
tains phenazopyridine hydrochloride it is co
dicated in glomerulonephritis, severe hepati
uremia, and pyelonephritis of pregnancy wi
disturbances.

Warnings: Safety during pregnancy not estab
Deaths from hypersensitivity reactions, agra
tosis, aplastic anemia and other blood dyscr
have been reported and early clinical signs
throat, fever, pallor, purpura or jaundice) ma
dicate serious blood disorders. Frequent CB
urinalysis with microscopic examination are
ommended during sulfonamide therapy.

Precautions: Use cautiously in patients with
paired renal or hepatic function, severe alle
bronchial asthma; in glucose-6-phosphate
dehydrogenase-deficient individuals in who
dose-related hemolysis may occur. Maintain
adequate fluid intake to prevent crystalluria
stone formation.

Adverse Reactions: *Blood dyscrasias* (agran-
ulocytosis, aplastic anemia, thrombocytope
leukopenia, hemolytic anemia, purpura, hy
thrombinemia and methemoglobinemia); *al*
reactions (erythema multiforme, skin erupti
Stevens-Johnson syndrome, epidermal necr
urticaria, serum sickness, pruritus, exfoliati
dermatitis, anaphylactoid reactions, periorbi
edema, conjunctival and scleral injection,
sensitization, arthralgia and allergic myocar
G.I. reactions (nausea, emesis, abdominal
hepatitis, diarrhea, anorexia, pancreatitis a
stomatitis); *CNS reactions* (headache, peri
neuritis, mental depression, convulsions, at
hallucinations, tinnitus, vertigo and insomni
miscellaneous reactions (drug fever, chills, t
nephrosis with oliguria and anuria, periarteri
nodosa and L. E. phenomenon). Due to cert
chemical similarities with some goitrogens,
uretics (acetazolamide, thiazides) and oral h
glycemic agents, sulfonamides have caused
instances of goiter production, diuresis and
glycemia. Cross-sensitivity with these agents
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painful phase of urinary tract infections. *Usu*
adult dosage: 2 Gm (4 tabs) initially, then 1
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causes other than infection should be sought
After relief of pain has been obtained, conti
treatment with Gantanol (sulfamethoxazole)
be considered.

NOTE: Patients should be told that the oran
dye (phenazopyridine HCl) will color the uri

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ing 0.5 Gm sulfamethoxazole and 100 mg
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atients should undergo a careful medical history and hysical exam. Primary medical disease should be valuated and treated. Particular emphasis should be laced on evaluating intraocular pressure to rule out arrow angled glaucoma; thyroid function; cardio-espiratory function and urinary function. A basic aboratory screening battery will include an EKG, thyroid rofile, SGOT, alkaline phosphatase, bilirubin, serum roteins, calcium and phosphorus, uric acid, BUN, omplete blood count and urinalysis.

With the exception of lithium carbonate, all mood ltering agents have some degree of anticholinergic side ffects. Those with the highest degree of anticholinergic ide effects include amitriptyline, imipramine and the onoamine exidase inhibitors (MAOI's). Those of the owest incidence of anticholinergic side effects include esipramine, nortriptyline and protriptyline.

Lithium carbonate has been implicated in producing ypothyroidism in more than 10 percent of patients. In ddition, modest hand tremor, diarrhea and polyuria are ommon.

Explain that patients may feel worse during the first week of drug administration. These typically transient ide effects are signals that the drugs are operating and aking effect.

All of the mood-modifying agents will require from hree to six weeks to take full effect. The first positive ffect will be normalization of sleep and appetite. Later, nergy levels will be restored and finally, the patient will egin to show greater initiative.

Atypical mood disorders associated with hypochon-driacal complaints, anxiety and excessive interpersonal dependency might prove responsive to MAOI's. In ddition, patients with specific phobias have responded well to these agents. Such patients should be cautioned regarding the use of psychostimulants, local anesthetics, decongestants as well as tyramine-containing foods. These latter foods include aged cheeses, pickled herrings, broad beans, chocolate, chicken liver and Chianti wine. MAOI's should not routinely be administered with concomitant tricyclic antidepressants. Psychiatric consultation is warranted prior to the use of these agents.

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Retroperitoneal Fibrosis:

Case Presentation and Review of the Literature

James E. McComb, M.D.
Eric P. Gall, M.D., FACP

INTRODUCTION AND CASE PRESENTATION

Since the initial description in the English literature by Ormond in 1948,[1] over 300 cases of retroperitoneal fibrosis have been reported. These may be categorized into primary (idiopathic) and secondary (those due to drugs, injury, tumor, etc.) types. The largest known cause of the secondary disease has been due to methysergide (Sansert®) administration for migraine headaches.[2] Literature is scanty in the area of proper diagnosis and management of patients with idiopathic retroperitoneal fibrosis. The following patient led us to review the literature and summarize what we feel is the best approach to this subject.

Case Report

H.H., a 50-year-old white man from Michigan, developed vague lumbar and abdominal pain in 1971 at the age of 43. He had never smoked cigarettes and denied exposure to ergot alkaloids, methysergide, amphetamines, or polyvinyl chloride. His previous health was excellent. His symptoms progressed over the next 2 years, he developed severe fatigue, nausea and had an 18 lb. weight loss. In 1974, after an upper gastrointestinal x-ray and barium enema were normal, an inconclusive exploratory laparotomy was performed. He was referred to the Mayo

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From: University of Arizona Health Sciences Center and Tucson V.A. Hospital. (Dr. McComb) Fellow in Rheumatology. Associate Professor Section of Clinical Immunology, University of Arizona College of Medicine. (Dr. Gall.)

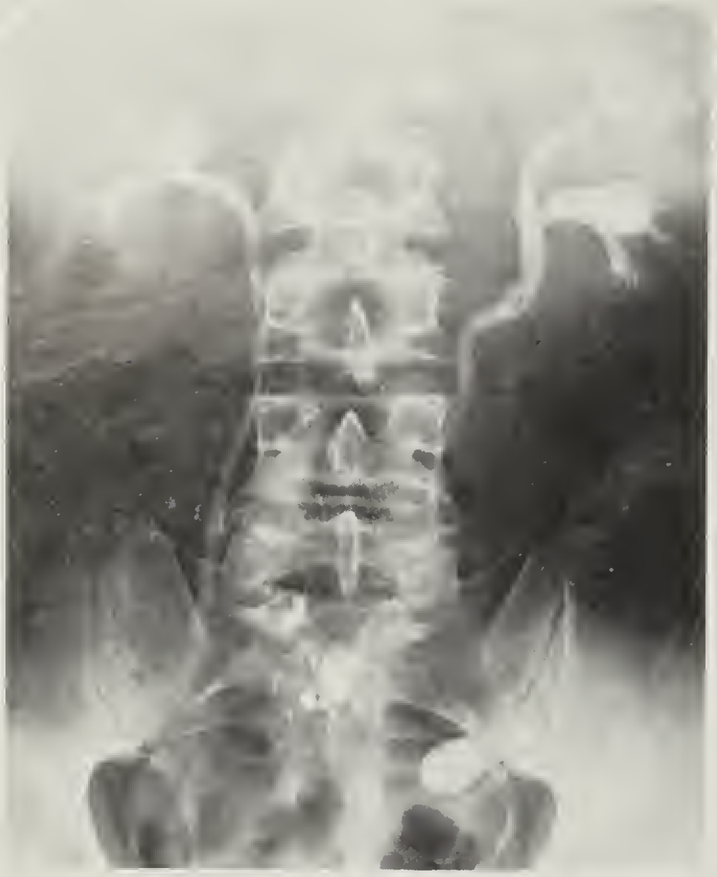

FIGURE 1

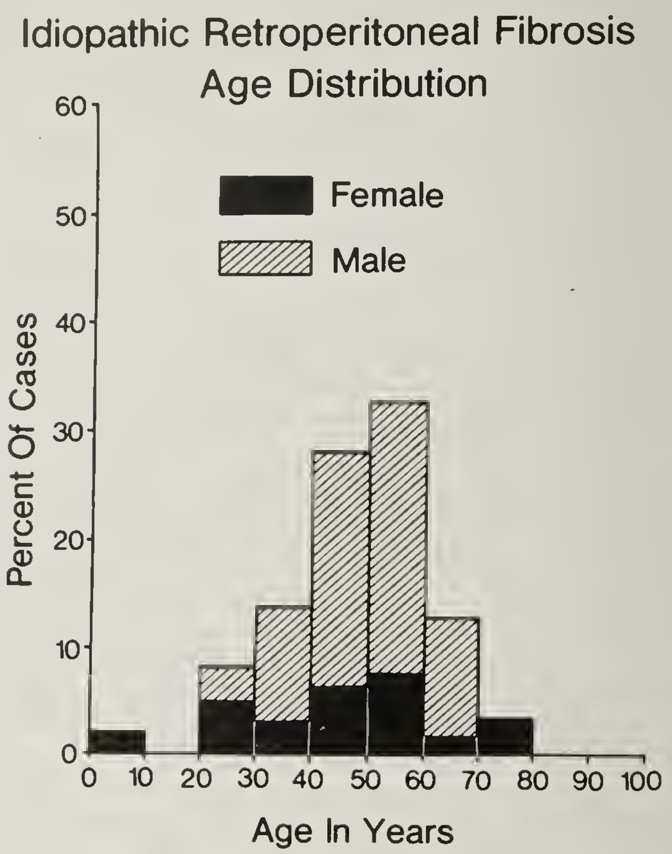

FIGURE 2

Clinic because of continued symptoms. In January, 1975 laboratory studies revealed a Hgb. of 13.7, sedimentation rate (Westergren) of 39 mm/hr., and normal BUN, creatinine, SGOT, Alkaline Phosphatase and LDH. An intravenous pyelogram (IVP) see Fig. 1) demonstrated medial deviation of both ureters with no visible peristalic motion.

In February, 1975 he underwent a second laparotomy, which revealed an intense inflammatory reaction and fibrosis surrounding the aorta from the inferior border of the pancreas to the bifurcation (8 cm). The aorta was encased in the fibrous tissue and the inferior vena cava deviated to the midline.

The patient was begun on 120 mg. of prednisone per day during the third post-operative week and noted progressive relief of pain. The dose was gradually tapered to 20 mg. twice daily, but attempts to withdraw steroids later resulted in recurrence of his symptoms. An IVP performed one year after his surgery showed normal ureteral position and function. The Prednisone dosage was slowly tapered over the next 6 months and finally discontinued by August of 1976. He since has had some mild symptoms of abdominal and back pain which have been controlled with analgesics. His most recent IVP in December, 1977, was normal. Laboratory studies revealed normal urinary sediment, renal function studies, and erythrocyte sedimentation rate in June, 1978.

Clinical Description

Idiopathic retroperitoneal fibrosis is a disease chiefly affecting middle-age individuals. Age and sex distribution as reported by Packham et al. in 138 patients is summarized in Figure 2.[3]

The lesion of retroperitoneal fibrosis is a non-encapsulated fibrous plaque that may be localized to th retroperitoneal area or in some cases involve th mesentery, pelvic structures and mediastinum. In it initial stage one may find subacute inflammation whic then progresses to hyalinized fibrous tissue.[4,5] The diseas process almost always involves one or both ureters, bu may also encase the great vessels, lumbosacral nerv roots, sympathetic plexus, bowel, or mesentery, producing a wide range of signs and symptoms. These includ anuria, sciatica, claudication, impotence, bowel obstruction and intestinal infarction.[3,4] Bilateral ureteral involvement is usually seen, but unilateral disease has bee reported. The initial clinical presentation is usually vagu and may include symptoms such as abdominal or lumba pain, fatigue, nocturia, and nausea. Oliguria an azotemia have been on occasion the first signal of th process.[3] In one series of 40 patients, from Great Britain 38 had azotemia and hypertension secondary to obstructive uropathy at the onset.[6] Half of the patients ha diastolic blood pressures of greater than 100 mm Hg There was a direct correlation between the degree o blood pressure elevation and the degree of renal failure.

Laboratory Diagnosis

Laboratory findings in retroperitoneal fibrosis are ofte normal. There are no specific tests. Acute phase reactant are elevated in the active phase of the disease, and rena function studies reflect insufficiency produced whe ureteral obstruction occurs. In the previous series of 4 cases, mild anemia was found in all cases, elevated whit lood counts in 50 percent, elevated BUN and creatinine 40 percent, and abnormal urinalysis with diminished ecific gravity, white and red cells and mild proteinuria 58 percent.[6] The sedimentation rate is elevated[8,9] and ppears to correlate with the activity of disease.[7] adiographic procedures, such as IVP and retrograde rography, best define the ureteral lesion,[10] but definitive iagnosis can only be made with exploratory surgery and iopsy.[5]

tiology and Pathogensis

Because of its association with diseases believed to be utoimmune in etiology, such as Riedel's struma, clerosing cholangitis, and rheumatoid arthritis, extensive erologic studies have been done in patients with retro-eritoneal fibrosis.[11] However, antinuclear antibodies, .E. preps, rheumatoid factor, cryoglobulins, and comple-ient levels, have been normal and immunofluorescent :ains on biopsy specimens have been negative.[5,6,12] The ifferential diagnosis of this entity is lengthy (Table 1). 'his is in part due to the vague onset and lack of specific iagnostic procedures other than biopsy. This definitive rocedure is often delayed.

The etiology of retroperitoneal fibrosis remains ob-cure. It was felt in the past that the process was econdary to chronic or recurrent infection or inflamma-ion in the urinary tract or bowel drained by the retro-eritoneal lymphatics, but observations have failed to ubstantiate this theory.[8] There has been no consistent emonstration of autoimmune phenomenon in patients vith retroperitoneal fibrosis. One of the most intriguing heories centers about the observation that the early esions of retroperitoneal fibrosis are virtually identical to hose seen in Weber-Christian disease, and that patients nanifesting both diseases have been described.[13] There re several reports of retroperitoneal fibrosis and clerosing panniculitis in patients with pancreatitis or ancreatic pseudocyst.[14] It has been postulated that elease of pancreatic enzymes or drainage from foci of nflammation into the retroperitoneal lymphatics with ubacute pancreatitis could produce necrosis and inflam-nation with subsequent retroperitoneal fibrosis.[13]

Retroperitoneal fibrosis has clearly been associated with he administration of ergot derivatives (ergotamine artrate, ergot alkaloids), ingestion of ergot-contaminated vheat, use of LSD (an ergot derivative), alpha-methyl-opa, and methysergide.[2,15,16] All of these drugs alter ascular tone and/or permeability via catecholamine or erotonin effects, and presumably produce a fibrotic eaction in susceptible individuals.[7] Both LSD and nythysergide (Sansert®) have been implicated in fibrosis f the heart, lungs, great vessels, pleura, and gastro-ntestinal tract.[2,15] Increased serotonin levels in carcinoid yndrome are associated with endocardial and pulmonary ibrosis.[18] Another hypothesis suggests that ergot alka-oids act as a haptene initiating a hypersensitivity reaction hat leads subsequently to fibrosis.[8] Without evidence of n autoimmune process, this seems unlikely.

TABLE 1
DIFFERENTIAL DIAGNOSIS
OF RETROPERITONEAL FIBROSIS

Retroperitoneal tumors:	Sarcoma Lymphoma Hodgkin's disease Pancreatic carcinoma Metastatic carcinoma
Ureteral or renal calculi	
Carcinoma of the ureter or kidney	
Infectious processes:	Tuberculosis Pancreatic pseudocyst Retroperitoneal abscess Diverticulitis Appendiceal abscess
Inflammatory connective tissue diseases:	Polyarteritis nodosa Weber-Christian disease Chronic pancreatitis
Aortic aneurysm	

Treatment and Prognosis

The prognosis of retroperitoneal fibrosis is related to the degree of renal insufficiency and hypertension which occurs.[6] The mortality is approximately 12 percent, with death usually due to renal failure or malignant hypertension.

Therapy for this disorder has been surgical, with lysis of fibrotic tissue encasing the ureters and great vessels.[9] Administration of moderate doses of corticosteroids in uncontrolled studies was thought to be effective in arresting on reversing the fibrotic process.[19,20] By following the erythrocyte sedimention rate and pyelograms as necessary, the physician should adjust the steroid dose to the minimum required to control the disease.

Inciting drugs (ergot derivatives, methysergide, LSD, alphamethyldopa) should be discontinued and may be associated with some reversal of the disease process, but symptomatic therapy with analgesics may be required.[2,21]

Thus retroperitoneal fibrosis is a disease of unknown etiology causing entrapment of viscera in a fibrous mass. It may be associated with ingestion of certain drugs and should be treated by discontinuing any medication implicated and with surgery and/or steroids when indicated. Careful attention to renal failure and hypertension is requisite.

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Surgery

The Surgical Treatment of Pancreatic Disease

C. Herbert Fredell, M.D.

The treatment of pancreatic disease ranges from skillful neglect to ultra radical surgery. The unpredictability of the clinical course of pancreatic disease is well known.[7-15] The onset of fulminating acute pancreatitis after an apparently routine operation on the biliary tract or stomach gives pause to our certainties when confronting pancreatic disease surgically. The multitude of operative procedures described for chronic pancreatitis testify to the complexity of the problem and the frustration of the surgeons treating it. The dearth of cures of adenocarcinoma of the pancreas has stimulated several attempts at earlier diagnosis and controversy over the proper

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From: Flagstaff Hospital, Flagstaff, AZ, Dr. Fredell, Chief of Surgery.

surgical management of the problem.[7]

This paper will not review the literature on the many controversial aspects of pancreatic disease. A few pertinent references will be cited and an experience gained over a period of seventeen years in a small hospital will be presented.

During this period of time four general surgeons performed all of the operative procedures and consulted on the majority of the non-operative patients. The surgical approach to pancreatic disease has been conservative when dealing with pancreatitis and pancreatic malignancy. Resection of the pancreas was done infrequently for severe forms of pancreatitis and has not been done for malignancy.

Pancreatic injury and adjacent organ diseases have required the majority of the resection procedures. Infrequent encounters with some of the pancreatic surgical problems has influenced this group of surgeons to be more conservative than necessary in some cases.

Materials and Methods:

A retrospective analysis of the records of 252 cases of pancreatic disease discharged from the Flagstaff Hospital from 1-1-61 to 1-1-78 was done. The age distribution was from 10 months to 92 years of age with an even distribution decade by decade from ten to seventy. There were 138 males and 114 females. The most common presenting complaint was abdominal pain in 140 cases. Biliary tract disease was present in 49 cases, alcoholism in 35 cases, jaundice in 25 cases, and the patient was postoperative in 18 cases. Seventeen patients had calcifications seen on abdominal x-ray film.

The most common diagnosis was 201 cases of pancreatitis. (Table I) The diagnoses and treatments have been summarized. (Table II) The results of the surgical procedures have been summarized. (Table III) It is of note that the postoperative complication rate was high. The postoperative deaths were due to sepsis in the majority of cases. (Table IV)

Comment:

During the period of time from 1961 to 1978 there were 76,712 patients discharged from the Flagstaff Hospital. There were 2,352 patients discharged with the diagnosis of diabetes as a primary or secondary diagnosis. In contrast, we have found 252 cases of pancreatic disease that required surgical consultation or treatment during that time. There were 104 cases that required surgical treatment. There were 9 postoperative deaths among these cases. (8.6%)

The morbidity following pancreatic surgery has been high. Six pancreatic fistulas occurred postoperatively. Two of these required surgical excision and pancreaticoenterostomy. There were six intraperitoneal abcesses. Two of these were primary in the pancreas secondary to common duct stone with rupture. There were six wound complications and 3 cases of massive postoperative intraperitoneal bleeding. There were 4 cases of severe postoperative pulmonary complications. Death was due to sepsis in 5 of the 9 patients. The longest survival with carcinoma with biliary enteric bypass was 30 months and the shortest 1 month.

Table I

THE SURGICAL TREATMENT OF
PANCREATIC DISEASE
Flagstaff Hospital
1-1-61 to 1-1-78

Diagnosis	**252 Cases**
Atrophy	1
Ectopia	6
Annular Pancreas	1
Abcess	3
Trauma	11
Pancreatitis	
Acute	113
Acute Recurrent	33
Hemorrhagic	5
Necrotizing	2
Chronic	48
Islet Cell Hyperplasia	1
Carcinoma	28

Discussion:

The three most common conditions associated with pancreatitis are biliary tract disease, alcoholic intake, and postoperative states following gastric and biliary tract surgery. The pathophysiology of acute pancreatitis entails pancreatic secretions gaining access to the interstitial tissue of the gland and initiating a spectrum of catalytic and autodigestive enzymatic changes. The early phase of the disease is characterized by interacinar edema, hence, the term acute edematous pancreatitis. This phase is usually a self-limited benign disease which occasionally progresses to a fulminant and often fatal process. Because of this relationship, a surgical awareness must accompany the management of pancreatitis from its onset.[17]

Ranson et al[20] correlated 11 clinical factors present within the first 48 hours of the disease, with an increased morbidity and mortality. He recommended peritoneal lavage when the patient failed to respond to the usual measures. If response to lavage was not good, a laparotomy with drainage of the peripancreatic area, gastrostomy, cholecystostomy, and feeding jejunostomy is recommended.[13] If pancreatic necrosis is present, a subtotal pancreatectomy should be done.[18]

If a patient survives the episode of acute pancreatitis, an infrequent complication of pseudocyst formation may occur.[14] It usually occurs when there is ductal disruption or acinar injury. It may follow pancreatic trauma or malignancy formation. The pseudocyst is usually palpable and may have atypical location or presentation. There may be jaundice, gastrointestinal hemorrhage,

Table II

THE SURGICAL TREATMENT OF PANCREATIC DISEASE
Flagstaff Hospital
1-1-61 to 1-1-78

Diagnosis	251 Cases	Treatment
1. Atrophy	1	1 None
2. Ectopia	6	6 Excision
3. Annular Pancreas	1	1 Duodenojejunostomy
4. Abcess	3	2 Drainage and Common Duct Exploration
		1 Drainage
5. Trauma	11	1 Observation
		6 Drainage
		4 Drainage and Suture
6. Pancreatitis		
Acute	113	112 Non-surgical
		1 Exploration
Acute Recurrent	38	29 Biliary Tract Surgery
		5 Exploration and Drainage
		2 Exploration
		1 Biopsy
		1 Jejunostomy
Hemorrhagic	5	3 Non-surgical
		1 Gastrojejunostomy
		1 Exploration and Drainage
Chronic and	48	
Necrotizing	2	30 Non-surgical
		8 Cystoenterostomy
		4 Pancreatectomy
		2 Biliary tract surgery
		2 Biliary enterostomy
		1 Cyst excision
		1 Cyst drainage
		2 Drainage of pancreas
7. Islet Cell Hyperplasia	1	1 Pancreatectomy
8. Carcinoma	28	6 Non-surgical
		10 Exploration and biopsy
		12 Biliary enteric bypass

ascites, pleural and mediastinal effusions, or cervical mass.[6] The amylase determination of the serum, urine and the cyst fluid are usually elevated. The abdominal echogram or scan has been helpful in making this diagnosis.

The treatment of pseudocyst is observation or surgical intervention. While one-fourth will regress spontaneously, the complications of hemorrhage, perforation, and infection can occur in the cyst. In the absence of resolution, surgical drainage or excision should be done. Internal drainage is desirable if the cyst wall is mature enough to permit anastamosis to the stomach or jejunum. A biopsy of the cyst wall will assist in making an accurate diagnosis.[14]

Pancreatitis is a recurring and progressive disease in a large number of those afflicted. If coexistent disease is correctable, it may decrease the recurrence rate.[6] Alcoholism is the main cause of chronic forms of pancreatitis. Abstinence is the only solution to that problem.[15] Usually the patient is plagued with abdominal pain, weight loss, steatorrhea, and diabetes mellitus. Pathologically the pancreas contains fibrosis, ductal dilatation with areas of stenosis, calcium deposits, and atrophy of the islet cells. The recurring episodes of pancreatitis are related to partial intermittent bouts of ductal obstruction. This in turn produces more duct stenosis and perpetuates the disease.[6]

The surgical treatment of chronic pancreatitis is directed at the other organs that are related to the recurring disease as well as directly at the pancreas. Biliary tract disease with involvement of the sphincter of Oddi is treated by cholecystectomy and sphincteroplasty. Duodenal ulcer disease when present should be treated.for cure. Duodenal stenosis will require a gastrojejunostomy and hyperparathyroidism is treated by parathyroidectomy.

When there are no unrelated organ diseases, the surgical treatment is directed to the pancreas. Sphincteroplasty with pancreatography and ductal exploration with stone removal is often helpful. Longitudinal pancreatorraphy with pancreaticojejunostomy, pancreatic resection with pancreaticojejunostomy, and subtotal pancreatectomy[18] have each been described as the procedure of choice.

When all measures to alleviate pain have failed and narcotic addiction is prevelant, a splanchnic nerve resection may help.[15]

It is important to note that a basis for a particular surgical procedure should exist. Preoperative endoscopic retrograde cholangiopancreatography[4] or pancreatography[6] at the time of laparotomy is most helpful in that regard. The surgical assault should occur during a quiescent phase of the disease with the patient in good nutritional status. Hyperalimentation may be necessary preoperatively.[5] At the time of surgery, the procedure with lowest risk which is the least extensive, which gives a reasonable chance of relieving symptoms is the one of choice. The ultimate solution to pancreatitis is total pancreatectomy[11, 18] but the diabetes and enzyme insufficiency do not justify such radical treatment for nonmalignant disease.

Pancreatic injury occurs with either blunt or sharp abdominal trauma. It may coexist with other organ injuries or may occur as an isolated injury. Occasionally the pancreas is injured in the course of other abdominal surgery. Anane-Sefah et al[1] reported 50 cases of pancreatic injury with a 14% mortality. There was a 70% postoperative morbidity. He contrasted the drainage procedure versus the resection procedures and concluded

TABLE III
THE SURGICAL TREATMENT OF PANCREATIC DISEASE
Flagstaff Hospital
1-1-61 to 1-1-78

gical Treatment — 104 Cases

cedure	Cases	Complications	Cases	Deaths	Cases
ary tract incterot-4) Common Duct ploration)	33	Wound infection Cholangitis Abcess Pneumonitis	3 2 1 1		
ary enteric Anastamosis	14	Atelectasis	3		
ploratory Lap	3				
with Biopsy	11			Hem. Pancreatitis	1
with Pancreatic Drainage	15	Abcess Hemorrhage Fistula Duodenal Obstr'n Wound Infection	4 2 3 1 1	Sepsis Mesen. Thrombosis & sepsis Sepsis	2 1 1
odenojejunostomy	1				
strojejunostomy	1				
unostomy	1				
cision Pancreatic Ectopia	6				
ture of Pancreas & Drainage	4	Fistula Hemorrhage	2 1		
ncreatic Cyst Excision	1	Fistula	1		
ncreatic Cyst Drainage	1	Recurrent Pan.	1		
ncreatic Cystoenterostomy	8	Pleural effusion Liver failure Pseudocyst	1 1 1	Pulm. Embolus	1
rt. Pancreatectomy with enterostomy	3	Recur. Pan. Disrupt. Anast. Recur. Pan.	2 1 1	Sepsis C.V.A. Anaphylaxis	1 1 1
with drainage	2				

hat the perforations of the body and tail of the pancreas hould be resected. If the duct is intact with an injury of he head of the pancreas, a sump drainage is adequate. If devitalizing injury of the head of the pancreas and luodenum occurs, a pancreaticoduodenectomy will be necessary.

Carcinoma of the pancreas has a bad prognosis in the best of surgical centers. Lesions of the ampulla of Vater and duodenum have often been lumped in those reported eries so that one gains a more optimistic opinion about carcinoma of that region.[2] Shapiro[22] collected 496 cases rom seventeen series of reported cases of carcinoma and noted an operative mortality of 21% for pancreaticoduodenectomy and the five-year survivors to be 4% of cases. If the Mayo Clinic results[19] are excluded from another gathering of twenty series of cases[7] totalling 703 cases of pancreaticoduodenal resection, one finds a 1% cure rate. In the compilation there was a 32.1% operative and postoperative mortality rate. Warren has reported some of the most optimistic opinions concerning pancreaticoduodenectomy at the Lahey Clinic. For some reason, yet unclear, their results and the results of the Mayo Clinic cannot be duplicated by surgeons elsewhere.

The average survival of a good risk patient with nonmetastatic disease who is treated with a biliary bypass instead of a pancreaticoduodenectomy is 12 months. When a patient perishes from a pancreaticoduodenectomy one year of life that could have been expected following bypass is sacrificed. On the average, when a patient survives pancreaticoduodenectomy, he lives 10 years. Against these ten patient years of life gained there is a loss

Table IV
SURGICAL DISEASES OF THE PANCREAS
Flagstaff Hospital
1-1-61 to 1-1-78

Deaths:

1. A 27-year-old M. with blunt trauma to the abdomen with multiple intraabdominal injuries. A large hematoma of the pancreas was drained. Three weeks later death was due to peritonitis, abcess and mesenteric thrombosis.
2. A pancreatic mass was noted at time of laparotomy. Needle biopsy was followed by death 8 days later due to hemorrhagic pancreatitis.
3. Acute hemorrhagic pancreatitis was found at laparotomy. Cholendochotomy, drainage of the pancreas, and jejunostomy were done. Duodenal obstruction required a gastroenterostomy. Three weeks later death was due to sepsis.
4. Acute pancreatitis was discovered at laparotomy. Drainage and cholecystostomy were done. Pneumonitis, intraperitoneal abcess, and uremia caused death 2½ weeks later.
5. A large pancreatic cyst was drained into the stomach. 24 hours later death was due to pulmonary embolism.
6. A partial pancreatectomy for cyst was done. Postop abcess developed and was drained 1 week later. Two days after the drainage a C.V.A. caused death.
7. A chronic necrotizing pancreatitis was discovered at laparotomy. Drainage of the pancreas, choledochotomy, gastrostomy, and jejunostomy was followed by massive hemorrhage 8 days later. Subtotal pancreatectomy was done. Sepsis and inanition caused death 3 weeks later.
8. A partial pancreatectomy for cyst was done. Heparin was given postoperatively. Anaphylactic reaction and death followed.
9. A 78-year-old woman had choledocholithiasis with rupture of the common duct and pancreatic abcess. Choledocholithotomy and drainage of the abcess was followed by sepsis, pneumonitis and uremia and death 4 weeks later.

of 26 to 32 patient years of life as a result of the deaths following this radical surgery. Most of the patients survive the operative procedure of biliary bypass and an occasional one has survived over five years. This evidence does not support the routine use of pancreaticoduodenectomy for operable carcinoma of the pancreas.[7]

Other surgical diseases of the pancreas are the tumors of the islet cell tissue.[8] Excessive production of insulin from beta cells may occur in instances of hyperplasia or insulinoma formation. They may be solitary or multiple. Occasionally they are malignant tumors. The presence of Whipple's triad of symptoms is classical when accompanied by serum insulin levels and C-peptide analysis. Arteriography will localize some lesions. When operative location of the problem is difficult, a blind subtotal pancreatectomy may be necessary.

Pancreatic cholera is a condition of watery diarrhea, hypokalemia and achlorhydria. It may be associated with benign and malignant tumors of the pancreas, adrenal, pulmonary or retroperitoneal region. The spectrum of symptoms is due to a vasoactive intestinal polypeptide.[12] The symptoms often respond to steroid therapy. If response is poor and recurrent, a surgical search may be necessary.

Additional pancreatic lesions that require surgical treatment include cystadenoma, cystadenocarcinoma,[3] cystic leiomyosarcoma, cystic rhabdomyosarcoma, and cystic islet cell tumor. Pancreatic resection is the treatment of choice. Occasionally duodenal obstruction in an infant may be due to annular pancreas which will require bypassing the lesion.[10]

Summary:

1. Surgical treatment of pancreatic disease includes operative procedures on the biliary tract, the gastrointestinal tract, the parathyroid glands, and the sympathetic nervous system. The involvement of the mediastinum and pleural space also entails procedures in that area of the body. The surgical procedures directed to the pancreas gland range from simple drainage to ultra radical excisional procedures. The role of alcohol and the desirability of abstinence when pancreatic disease is present cannot be overemphasized.

2. A seventeen-year experience in a small hospital with the surgical treatment of pancreatic disease has been presented. 103 cases required surgical treatment with a 8.7% postoperative mortality rate. The morbidity rate has been high for some specific problems requiring surgical treatment.

3. During this period of time the approach to severe forms of pancreatitis has been conservative. All cases of hemorrhagic pancreatitis, whether they were treated nonsurgically or surgically, died. The involvement of a surgeon with a patient early in the course of the treatment of acute pancreatitis is desirable. A more aggressive surgical attitude toward the unresponsive case of pancreatitis is recommended.

4. Carcinoma of the pancreas continues to be a bad disease. Earlier diagnosis, if possible, would be helpful. Efforts continue with various methods to achieve this. Results to date are disappointing. Chemotherapy has not achieved its expected success. Radical surgery, done in highly selected cases, continues to offer the best hope of cure. The experience of this study substantiates our continuing reluctance to offer pancreaticoduodenectomy to patients with adenocarcinoma of the pancreas. There have been no operative or postoperative deaths among patients having carcinoma of the pancreas. Within the small hospital setting this is desirable.

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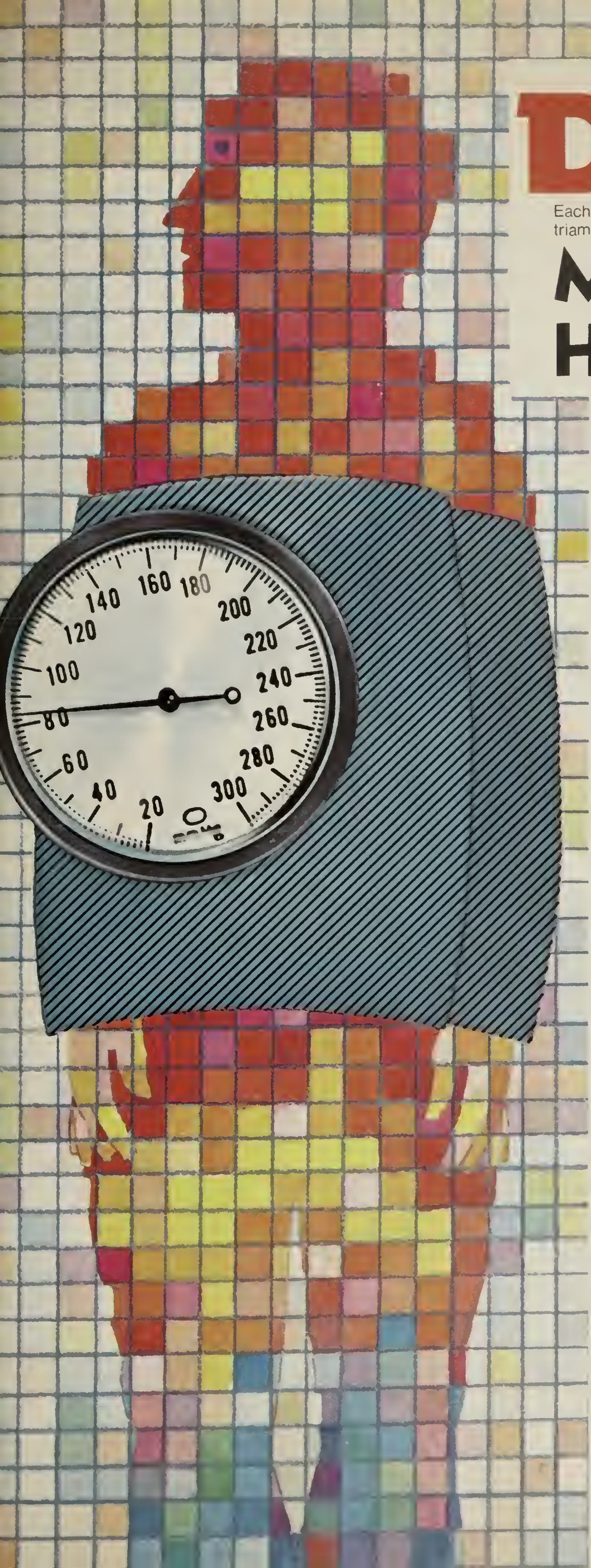

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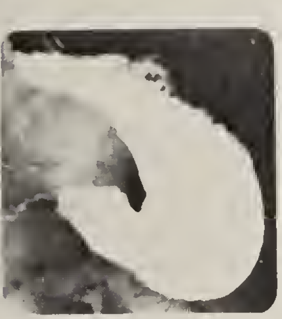
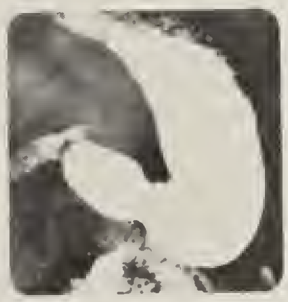


Pylorospasm has almost totally blocked passage of barium meal.



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King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964

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Usual Dosage Bentyl 10 mg capsule and syrup *Adults* 1 or 2 capsules or teaspoonfuls syrup three or four times daily *Children* 1 capsule or teaspoonful syrup three or four times daily *Infants* ½ teaspoonful syrup three or four times daily (May be diluted with equal volume of water) Bentyl 20 mg *Adults* 1 tablet three or four times daily Bentyl Injection *Adults* 2 ml (20 mg) every four to six hours intramuscularly only NOT FOR INTRAVENOUS USE MANAGEMENT OF OVERDOSE The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation Treatment should consist of gastric lavage, emetics, and activated charcoal Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested If indicated, parenteral cholinergic agents such as Urecholine* (bethanecol chloride USP) should be used

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Special Articles

Report of the First National Symposium On the Medical Uses of a Portable X-Ray Imaging Instrument:The Lixiscope

James W. Justice

Medical Uses for a Portable X-ray Imaging Instrument

The first symposium on the medical uses of the Lixiscope, a hand held, portable fluroscope, was held at NASA's Goddard Space Center in Maryland on July 27th and 28th, 1978. The name for this device is in part, an acronym for low intensity x-ray images, and was first reported by NASA in January, 1978.[1]

The Lixiscope is light weight, compact, rugged, and operates with only the 2.7 volts supplied by a button type battery which is also used in some electric eye cameras.

These features extend its function as a fluroscope to many diverse situations than possible for existing fluroscopes, from inspecting welds on pipeline projects in the field to the detection of art forgeries at the flea market.

The instrument was invented by an astrophysicist, Dr. Lo I. Yin, Goddard Space Center, for the purpose of gathering more precise data about the origin of gamma rays from deep space. The Lixiscope will be placed in earth orbit coupled with optical scanners to sweep the universe. The present limitations for medical use such as the small viewing area - only 20mm in diameter - and also the production of an inverted viewing image can be ascribed to the primary purpose for which it was invented. Therefore, as one speaker emphasized,potential medical users should not be constrained in their imagination by the configuration of the prototype instrument, but should understand the principles involved, specify their needs, and suggest changes in the design to accomplish the desired functions.

The Lixiscope is a package of thin discs that convert gamma or x-radiation into photoelectrons which are then cascaded or concentrated to bombard a phosphor screen to produce an image. The special component that concentrates the photoelectrons is called a microchannel plate. This part was developed by the U.S. Army Night Vision Laboratory in Fort Belvoir, Virginia, and is the limiting factor regarding the size of the viewing field. Millions of holes, each 12 microns in diameter are produced in a semiconductor material. (See Figure 1). Radiation first strikes a phosphor disc and is converted to photons. Photoelectrons are next produced by a photocathode. They then enter a thin fiberoptic disc colluminator. The photoelectrons next enter a high vacuum chamber and are both accelerated and multiplied through the microchannel plate. The average gain is approximatly

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From: Department of Health, Education and Welfare, Health Services Administration, Indian Health Service, Office of Research & Development, Tucson, Az 85734.

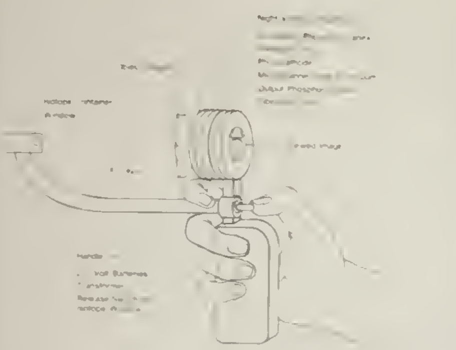


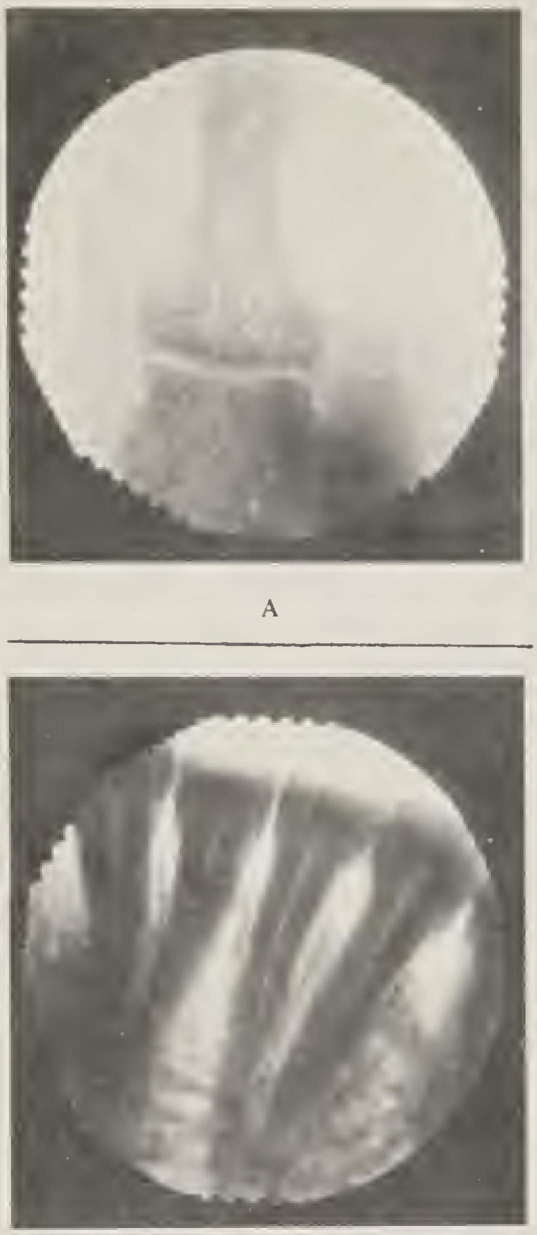
FIGURE 1
iematic drawing of protype Lixiscope, as
ıdified for dental use.

).[3] Finally, these concentrated electrons ıpact the second phosphor viewing reen. A second fiberoptic disc aids the ıal resolution of the image as seen by e viewer, or the camera.

The M.C.P. has also been anufactured with discs of 40mm and)0mm diameters, but there would ɪpear to be a size limit to which this ittle, delicate plate could be made before e Lixiscope would comprise its features ruggedness and portability. Also, the rger plates will undoubtedly be more pensive.

Drs. Richard Webber and John Gold of e National Institute of Health, branch r dental research reported their eliminary investigations with a special odel adapted for placing the radioactive urce within the oral cavity. These aptations were to decrease the size of e isotope container to about 1.5 cm ameter; change the mounting for the ntainer to a thin semi-flexible, movable d; and to remove the electronic lens hich produced an inverted image in the st model. The exact position of a file thin the root canal could be determined ıring root surgery. They, and all the vestigators used 50 microcuries of the dine isotope 125 for their terminations of the absorbed dose to e patient. This source delivered tween 27 and 30 KeV which produced a ›se of from 1.0 to 3.0 millirem per inute to the tissues. The effect of the acement of the gamma source within e mount, however, was also to limit the ›lume of tissue irradiated so that the tal tissue dose per minute would have een 1000 times less than with ›nventional dental x-ray equipment. he observer experienced no radiation ›sage from I^{125} since all rays were ›nverted to photoelectrons, and scatter as nil beyond the patient's oral cavity.

Dr. Alan Mishkin, University of onnecticut Health Center, School of ental Medicine, presented a comparison dental radiographs and poloroid film ctures from Lixiscope images. The solution of the current model may not fine enough to detect hairline actures, small apical abscess and other ›mmon dental pathology. These features demanded a resolution of more than 10 line pairs per mm, and the present Lixiscope produces about from 4 to 7 lp per mm.

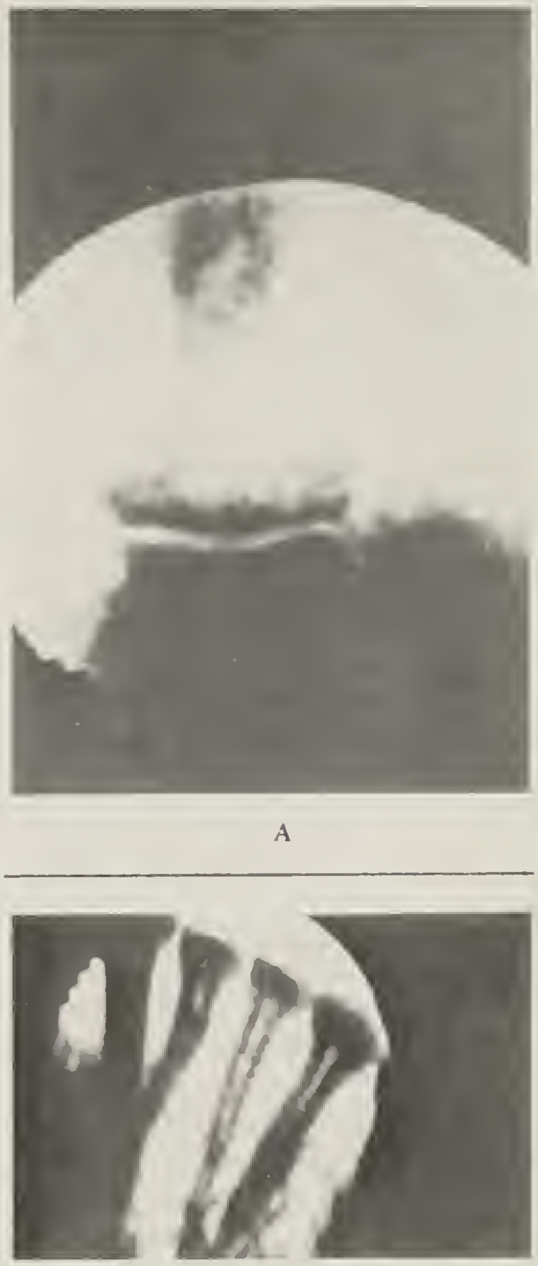


A

B

FIGURE 2
Image direct from Lixiscope photographed on black and white polaroid film. The image is magnified about 2.4 x larger than the object. White spots are artifacts from the film. A. Distal interphalangeal joint space. B. Root canals, lower incisors. The preceived image quality from the Lixiscope seemed better than these photographed images.

Dr. Thomas Spackman (Pediatric Radiologist from the University of Connecticut) conducted visualization trials using a 3000 gm rabbit to simulate a neonatal patient. His group was successful in locating the exact placement of endotrachial, intra arterial and esophageal tubes: catheters frequently used for neoonatal emergency conditions. He demonstrated that the gross condition of thoracic structures could be quickly visualized. He also suggested other uses for adult patients while undergoing surgery such as to place a sterilized Lixiscope within the abdomen to verify if the common duct, or ureters were free from stones, prior to closure. Radioactive material previously injected into a patient for diagnostic purposes could, following biopsy, be quickly evaluated to ascertain if the proper tissue specimen had been removed before the patient left the operating room.



A

B

FIGURE 3
Photographs of televized Lixiscope images from a standard black and white television monitor. A television camera with a close up lens was held against the Lixiscope screen. Transmission was by a direct TV cable. (Kodak Tri X film) A. Interphalangeal joint space. B. Root canals, incisors.

Doctors Press and Walters from the Department of radiology at Howard University, reported on the use of the Lixiscope in the emergency room for the clinical evaluation of hand injuries. He found that the penetration was not sufficient to evaluate foot injuries other than those involving the toes. Fractures and compression injuries of the digits were seen on the Lixiscope and verified by radiograms. However, the scope did not differentiate soft tissue injuries, except for one - presence or absence of foreign bodies.

Dr. Wiseman from the Pennsylvania

College of Podiatric Medicine reported similar findings but added that his group was able to ascertain whether the position of a needle was correctly inserted into a metacarpal joint before the contrast medium was injected. They were also able to determine that osteomyelitis was present in a digit after a 360° examination with the Lixiscope. Focal digital osteomyelitis can be missed because of the limited number of radiographs usually taken. He also suggested that due to the enthusiasm of the clinician during a Lixiscope examination, the patient may be exposed to more radiation than is necessary. An automatic timer should be added to the prototype model to warn the examiner after about 60 seconds.

Dr Simmons, from the Department of Laboratory Animal Medicine, Uniformed Services, University of Health Services, reported on the use of the Lixiscope to diagnose various fractures, to monitor callus formation in experiments regarding bone healing, and other uses in research. He doubted that this instrument would be commonly used by practicing veterinarians because of the cost.

Dr. Seltzer, co-developer of the Lixiscope from the National Bureau of Standards, and Dr. Yin summarized the present state of development. The cost of the components of the prototype Lixiscope was about $5000 plus the cost of the isotope, $800, but did not include the assembly which was done at the Goddard laboratory. The device is not being produced commercially, but the night vision component is available.

Experiments need to be done in the following areas: a more powerful isotope source with a longer half like than I 125 (60 days) needs to be found. Americium 241, cadium 109, and gadolinium 153 (with 242 days half life) are currently proposed for further studies. Various phosphor screens need to be tested with each isotope to find the best mix for improving resolution and contrast. The total resolution possible from the components of the night vision system should be about 30 line pairs per millimeter. However, the prototype Lixiscope (with the electronic lens removed) produces an image of about 7 lp/mm. The limiting factor at present is the type of phosphor screen used (Lanex). Experiments with cesium iodide phosphors are being conducted. Resolution and contrast may also be improved by aligning two microchannel plates so that the ratio of the channel diameter to the length of the tube can be increased. This will further cascade electrons and increase contrast. Experiments with computer image processing by attaching a plumicon tube to the phosphor screen may also increse contrast and resolution. Brightness can be increased by eliminating the aluminum coating on the fiberoptic plates. (This was a feature of the night vision component to prevent visible light feedback to the photocathode, but is unnecessary when an isotope is used for the photon source.) The complete proceedings of this symposium will be published by the Goddard Space Center, NASA.

It should be also suggested that controlled clinical research should be done to answer the question of whether rural general practitioners, pediatricians, nurse practitioners and physician assistants can more accurately diagnose fractures with the Lixiscope than by relying upon inspection and palpation alone. In rural medical practice, the standard x-ray equipment is often not readily available, and patients suspected of having fractures are sometimes put to unnecessary (in retrospect) travel and expense of receiving radiographic services.

The use of the Lixiscope in the hands of a non-physician practitioner and combined with a slow scan television system should also be explored. Last January, this writer was able to demonstrate the feasibility of transmitting clinically useful Lixiscope images via cable television at the NASA laboratories in the Johnson Space Center at Houston (Figures 2 and 3).

Our experiments at the Tucson Office of Research and Development of the Indian Health Service, DHEW, with the transmission of diagnostically valuable radiograph television images over ordinary long distance telephone lines from Sells, Arizona to Phoenix, Billings (Montana) and Houston (Texas) has demonstrated the value of the slow scan component.[2] It remains to be explored whether a remotely located radiologist or trauma specialist can accurately dignose Lixiscope images transmitted via telephone microwave television from a non-physician (or non-specialist physician) located in a rural health center without x-ray facilities.

The complete spectrum of beneficiaries from this invention is not yet imagined, but at present both patients and practitioners who live in rural areas, stand to gain from further development of the Lixiscope.

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State of the Art

Rheumatoid Arthritis: Concepts in Evolution

Eric P. Gall, M.D.
Edward A. Gall, M.D.
John T. Boyer, M.D.

While most physicians think of rheumatoid arthritis (RA) as an ancient disease, there is considerable evidence that it first emerged with the industrial revolution.[1] Skeletal remains show evidence of such other articular afflictions as gout, osteoarthritis, ankylosing spondylitis, etc., in ancient civilizations, but RA was first noted in remains dating from the 1700's. Osler in the first edition of his textbook of medicine (1892) described both "arthritis deformans" and "chronic rheumatism," which were, in truth, conglomerations of many different types of arthritis.[2] Standardized criteria for diagnosis of RA were not delineated until 1958.[3]

Many students of medicine consider the essence of rheumatoid arthritis to be synovial proliferation, "pannus," an "eating away at the joint." Indeed, this concept is still often taught. The present paper is intended to consider new aspects in the pathogenesis of this disorder. An understanding of this material is relevant to modern approaches to prevention and therapy of this destructive joint disease.

In 1931 it was recognized by Cecil that the sera of patients with RA caused agglutination of streptococci.[4] It was assumed by some that this organism was in some way responsible for the disease (much as in the case of rheumatic fever).[4] What was not appreciated at that time however, was that the streptococcal clumping was probably due to what we now know to be rheumatoid factor capable of agglutinating the gamma globulin coated bacteria; the organism itself acted much as does an inert particle. In 1948 Rose and others, using sheep red cells recognized that the common occurrence of a rheumatoid factor in RA reflected the existence of an anti-gamma globulin antibody.[5] Thus, the coating of particles by gamma globulin exposed new antigenic determinants on the gamma globulin molecule which would then react with the rheumatoid factor (R.F.). While R.F. measured in the clinical laboratory is mostly IgM antibody specific for antigenic IgG, its presence in an individual's serum is not specific for rheumatoid arthritis, being found in many other conditions and in some normal individuals.

In 1966 Hollander conceived a pathogenetic model for RA by observing cells containing immune complexes.[6] He also noted the injection of gamma globulin obtained from a rheumatoid patient in an unaffected joint of another person with this disorder caused the inception of overt arthritis localized in the new joint.[7] Gamma globulin from patients with conditions other than RA, i.e. degenerative joint disease and other inflammatory arthritides did not induce such an inflammatory process. A graphic representation of Hollander's hypothesis is shown in Figure 1. The theory suggests that immune complexes composed of gamma globulin, rheumatoid factor and complement are phagocytized by neutrophils and toxic products are then released and cause joint damage.

While Hollander's concepts have remained valid, it is now apparent that other factors are also involved in this mechanism. Much more has been learned about sequences within the model itself. Many patients in whom the rheumatoid factor is demonstrable do not get RA; indeed, it is also known that patients lacking measurable amounts of R.F. may exhibit overt RA. Using new methods not routinely available, anti-gamma globulins of the IgG and IgA variety have been detected in the serum of R.F. negative patients with RA.[8]

Let us now explore in some detail the rest of the pathogenetic sequence of joint destruction in rheumatoid arthritis. The complex interactions of these mechanisms suggests that there is much yet to be learned and that RA has a multifactorial causation leading to the final common pathway of joint destruction.

Initiating Factors: As previously mentioned, the streptococcus was considered implicated in this process.

From: University of Arizona Health Sciences Center, Tucson, AZ 85724. Dr. Eric P. Gall, Assoc. Professor, Internal Medicine, Clinical Immunology Section. Dr. Edward A. Gall, Distinguished Service Prof. Of Pathology (Emeritus) Univ. of Cincinnati College of Medicine. Dr. Boyer, Prof. of Internal Medicine & Chief Clinical Immunology Section U of A Health Sciences Center.

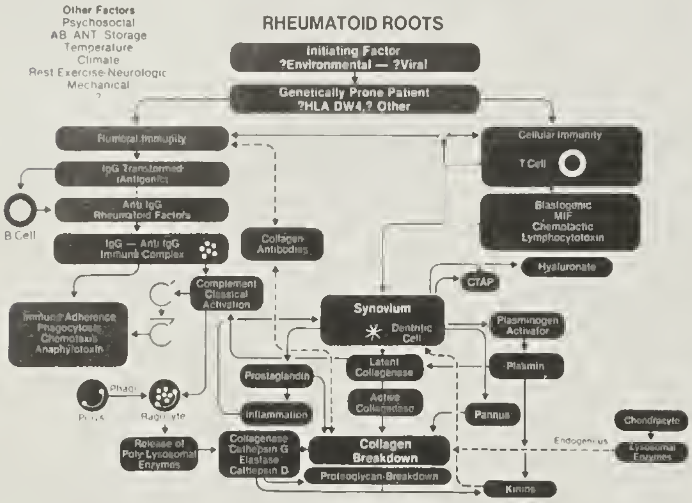

FIGURE 1
Model of pathogenesis of rheumatoid arthritis adapted from the concepts of Hollander, 1966.

Other bacteria have also been considered, although no consistent yield has been noted, nor have antibody titer elevations to bacteria been observed in RA. It has been shown that **Erysipelothrix indiosa** can cause a disease very similar to RA in swine.[9] Although the organism may be recovered early in the course, it disappears in later phases when only bacterial antigens can be isolated. These too eventually disappear, although the disease continues as a chronic destructive arhtritis. Despite its similarity to disease in man, human studies in early RA have failed to detect a like organism. Earlier reports suggesting mycoplasma as a contributing agent have not been confirmed, although certain animal models have exhibited a disease similar to RA. Arthritis is, however, a common manifestation of known mycoplasma infections.

Viruses have long been considered likely candidates in the initiation of RA.[9] Certain features in rheumatoid diseases are consistent with those encountered in slow virus infections. Once again, however, viruses have not been consistently isolated, nor have elevated viral antibody titers been a feature of most RA patients.[9]

One salient problem in the search for causative organisms has been a failure to pursue carefully a search in the early phases of rheumatoid disease (within days or hours of onset), and a possible disappearance or isolated storage of antigen after the disease has begun to progress. These would require prospective studies in cases with early, as yet undiagnosed acute synovitis. Schumacher, in early forms of arthritis found viral-like particles in the synovium of several patients.[10] These particles, however, could represent cell breakdown products, the appearance of which is often similar to that of known viruses. Sophisticated co-culture techniques, searches for viral DNA, reverse transcriptase and the determination of serologic titers for viruses have failed to show evidence of infection in patients with established disease.[9] Possibly the antigen is hidden from detection or having initiated immune activity, disappears without leaving a trace.

There is still much to suggest that a virus or other microorganisms play some part in the initiation of rheumatoid disease, but we do not yet know all the facets of infection-chronic immunologic disease interaction. Rubella and other viral exanthems of childhood often produce arthritis. In most cases this is short-lived, but in some progression to a rheumatoid- like disease has been observed.[9]

Genetic Factors: Another factor requiring pursuit is the matter of genetic predisposition to rheumatoid disease. Perhaps this and certain environmental factors (infection or other) are co-requisite to the initiation of RA. While ankylosing spondylitis and the axial arthropathies have a clear genetic basis, the statistical evidence for familial clustering is not as strong for RA.[11] There are occasional groupings of family members with the disease and there have been reports of twins suffering with RA.[12] On the other hand, the affliction is common, affecting from 2 to 3% of the population,[12] a fact which tends to negate this genetic implication. In early rheumatoid disease, the sex incidence is more or less equal. In its presistent form, however, the female has a 2:1 to 3:1 ratio of incidence to males. Other factors suggesting sex-linked or hormonal influence include the observation that rheumatoid disease tends to improve in young women during pregnancy.

Tissue culture studies with the synovium of rheumatoid patients have shown that cell growth is slower than in normal individuals.[13] Other investigators have shown that the plasma membrane of fibroblasts in the rheumatoid synovium has fewer marker enzymes such as 5 nucleotidase.[13] The cultures produce large amounts of underpolymerized hyaluronic acid but reduced amounts of chondroitin sulfate.[13] In addition, some hitherto undescribed proteins are found in the culture supernate. All these in vitro findings suggest genetic abnormalities or new host genetic control material not yet identified.

Analysis of human transplantation antigens on lymphocytes (HLA) in RA originally were found to be no different from the general population, but these initial studies were only done at the A, B, & C loci. More recently studies at the HLA-D locus, which require mixed lymphocyte cultures, have shown an unexpected preponderance of the type HLA-DW4 in about 30 to 60% of rheumatoid patients; it is present in 7 to 16% of control populations.[11] The prospective study of populations, such as that now in progress in Tecumseh, Michigan and Framingham, Massachusetts, is required.

Inflammatory Factors: Let us now look at the terminal sequence of the pathogenetic schema where there has been n explosion of knowledge in the past 5 years. It is now nown that inflammatory destructive substances are ecreted by 1) neutrophils, 2) lymphocytes, 3) syno-ium and 4) chondrocytes. Structural changes in cartilage uggest both endogenous and exogenous sources of nzyme production. The destruction of the joint is caused y proteoglycan (ground substance) depletion as well as ollagen degradation. These lesions are then made worse y mechanical disruption, pannus formation and ab-ormal forces due to malalignment.

The synovium in RA has been shown by Castor and olleagues to secrete a "connective tissue activating eptide (CTAP)" which inhibits synovial fibroblast lucose metabolism and adversely alters hyaluronate roduction.[14] Lymphocytes in the synovium are also nown to produce factors which stimulate collegenase roduction by synovial cells.[14]

Immune complexes recruit neutrophils and are ingested y them, causing release of certain lysosomal enzymes. At east four of these enzymes are known to be extruded by e polymorphonuclear cell and participate in joint estruction.[15] These include:

1) Cathespin G: Hydrolyzes cartilage proteoglycans and insoluble colagen.
2) Granulocytic collagenase: Cleaves native solubilized collagen into tropocollagen A+B.
3) Elastase: Along with collagenase, this enzyme attacks insoluble collagen and proteoglycans.
4) Cathepsin D: Attacks intracellular proteins and contributes to the formation of active kinins.

Dr. Gerald Weissman has been in the forefront in the tudy of these enzymes and in several fine articles has eviewed the function and release mechanisms.[15] Four nechanisms of enzyme release from the neutrophil have een established:

1) Cell death: Ingested particles cause plasma membrane damage with resultant cell death following which all intracellular enzymes and electrolytes are released. This only occurs to a minor extent in RA.
2) Perforation from within (suicide sac): By this mechanism crystals residing in phagolysosomes cause performation of sacs resulting in cell death.
3) Regurgitation during feeding: This occurs as the neutrophil ingests an immune complex into a phagosome and then combines with a lysosome to form a phagolysosome. The phagolysosome regurgitates its content from the cell, releasing lysosomal enzymes before the external portion of its membrane can close. The cell remains viable. Elastase and collagenase are known to be extruded in this manner by the polymorphonuclear leukocyte.
4) Reverse endocytosis: Enzymes in the lysosome are released while the cell attempts to phagocytize material on its surface. Phagocytosis really never occurs and the cell remains viable. Other cytoplasmic enzymes remain within the cell.

An understanding of these mechanisms helps one to think about pharmacologic control of enzyme damage. Various anti-inflammatory drugs are known to reduce the mechanisms cited in 3) and 4), increasing cyclic AMP and this stabilizing lysosomal membranes. In addition to this, some drugs cause disassembling of microtubules involved in the secretion of intracellular materials.[15]

It is known that chondrocytes in rheumatoid cartilage have decreased proteoglycan in their immediate vicinities.[16] These chondrocytes secrete lysosomal enzymes of their own and are thus more or less "self destructive." Muirden has shown that homogenates of articular cartilage contain increased cathepsin B and other enzymes of chondrocyte origin in RA.[17] Thus, the neutrophil and chondrocyte both contribute to joint destruction.

In recent years, Harris, Krane and others have learned a great deal about synovial cells and their role in joint destruction. They have observed that certain cells in monolayer cultures of rheumatoid synovium (but not the normal membrane) secrete collaganase precursors.[18] The collagenase secreting cells appear "dendritic" and seem to be relatively unique to RA.[18] Their number is directly related to the amount of collagenase precursors produced. Immunofluorescent staining of collagenase in dendritic cell granules is increased in most rheumatoid patients. The collagenase, once secreted, appears to be bound and inhibited by alpha$_2$ macroglobulin.[18] The entire complex may then bind to intact collagen, though not as well as to active collagenase itself.

Rheumatoid synovium also secretes plasminogen activator, which causes plasmin formation in synovial fluid. Plasmin will convert latent synovial collagenase to its active form whether or not it is bound by alpha$_2$ macroglobulin. Collagen is thus broken into monomers by activated synovial collagenase.[18] Plasmin also activates the complement system, which increases the intensity of inflammation. The heat generated by the inflammatory process may cause monomers to break down further into gelatin polypeptides. Indeed, with a temperature increase from 33°C to 36° (in RA) a four-fold rise in collagenase activity is observed.[14] Thus, part of the benefit of treatment by anti-inflammatory drugs in RA may reflect a lower intraarticular temperature. Cathepsin G, a neutral protease, and other peptidases then further degrade the gelatin polypeptides and there is urinary excretion of collagen byproducts. In addition, intracellular phagocytized collagen is broken down by lysosomal enzymes in the rheumatoid synovial cells and excreted in much the same way. Rheumatoid synovial fluid has an anaerobic metabolism, a low pO_2 and pH, an increase in pCO_2 and lactate, further enhancing the inflammatory process.

The microsomal fraction of rheumatoid synovium produces large amounts of prostaglandins.[19] These are formed by synovial lining cells, inflammatory cells, and even blood vessel endothelium. Besides causing the cardinal signs of inflammation, prostaglandins may affect bony lysis directly.[19] Their synthesis is controlled by prostaglandin synthetase enzyme which is inhibited by most nonsteroidal anti-inflammatory agents. Of these, aspirin appears to be least potent by dose when compared to phenylbutazone, ibuprofen, naproxen and indomethacin. Despite aspirin's weak inhibitory effect, its activity is irreversible; this may not be the case with other agents.[20] The effectiveness of aspirin is greatly improved in this manner. Steroids are also known to inhibit prostaglandin synthesis.[19]

Immunologic Mechanisms in Joint Destruction: Several investigators have now shown that antibodies other than rheumatoid factor occur in this disease. Recently, much attention has been given to the fact that antibody to collagen occurs in as many as 60% of rheumatoid patients and in fewer than 10% of controls.[14] These antibodies are directed in the main against type 2 and type 3 collagen. It is of further interest that delayed hypersensitivity to cartilage antigens is proportional to the amount of cartilage destruction.

Delayed hypersensitivity (T cell mediated) has received increasing attention. Rheumatoid synovium is infiltrated by lymphocytes and most of these are T cells, which produce many toxic lymphokines.[20] Some of those identified include blastogenic, transfer, macrophage inhibition, chemotactic factors and lymphocytotoxins. On the other hand, lymphocyte stimulation studies with cell mitogens have suggested decreased T cell reactivity. Skin tests are abnormal and there is often anergy in these individuals. Patients who undergo thoracic duct drainage, primarily a depletion of T cells, have sustained remissions.[21] With a reinfusion of lymphocytes or cessation of the duct drainage, the disease is reactivated.[21] Studies are now being performed using such immunostimulators as transfer factor and levamisole (in contrast to most drugs, which suppress the immune reaction).[22] Both agents have had success in treating rheumatoid patients. While one might think that immunostimulation would be specifically contraindicated in RA, the delicate autoregulatory balance between T and B cells may well be disturbed in this condition and stimulation of the defective controlling factors (suppressor cells) may cause remission of disease. All of these data suggests the existence of a defect in either T cells in general or at least certain subpopulations, probably suppressor cells. Other drugs such as cytotoxic agents and corticosteroids may suppress the entire immune system, but these unfortunately have a high degree of toxicity.

Other Mechanisms: Finally, there are a number of other mechanisms in the pathogenesis of RA worthy of brief mention. Once joint damage has begun, various mechanical factors including friction, malalingment, secondary degenerative changes and ligament and tendon ruptures contribute to progression of the disease. Though not primary factors, they are involved in the end product of deformity and crippling.

The basis for therapeutic efficacy of rest and exercise are not well understood.[7] Patients who have flaccid paralysis before the onset of their rheumatoid disease do not develop arthritis in the paralyzed limb.[22] Cerebrovascular accidents, poliomyelitis and other neurologic diseases have all been shown to confer a degree of protection against erosive disease in affected limbs.[23] It has been our own observation that in the few patients with spastic paralysis who have developed RA, the intensity of the arthritis has been significantly worse on the spastic side. Thus, there also appears to be a neurogenic influence on rheumatoid activity.

TABLE I
PATHOGENETIC MECHANISMS IN RHEUMATOID ARTHRITIS — THERAPEUTIC IMPLICATIONS

PATHOPHYSIOLOGIC EVENTS	RELATED THERAPEUTICS
Initiating factors	
Environment	Environmental manipulation
Viral	Antiviral agents
Genetic factors	
HLA DW4	?Genetic counseling or manipulation
Humoral immune system	
Rheumatoid factor and anticollagen antibody	Corticosteriods, cytotoxic agents
Cellular immune system	Corticosteroids, cytotoxic agents, levamisole, transfer factor
Complement	Gold, cobra venom factor, oxidizing agents
Neutrophils	Cytotoxic agents, membrane stabilizers (gold, penicillamine, corticosteriods, antimalarials, etc.) ?antienzymes
Synovial enzymes	Membrane stabilizers, surgery, ?antienzymes
Chondrocytes, cartilage	Surgery
Prostaglandins	Nonsteroidal anti-inflammatory agents, aspirin, corticosteroids
Cartilage storage	?catharsing agents, surgery
Temperature effects	Anti-inflammatory agents
Neurologic-rest-exercise	More scientific resting of joint
Mechanical factors	Surgery, physical therapy, splinting
Climate	Southwestern United States
Other factors	Research

Here in Arizona, there has been a great deal of interest in the effect of climate on arthritis. Suffice it to say that climate has no bearing on the longterm course of rheumatoid arthritis, but when sudden decreases in barometric pressure are associated with a simultaneous increase in humidity, the disease flares briefly. Some patients who move to the stable climates in the southwest report subjective improvement in their symptoms.

In an attempt to determine why certain joints are affected and not others and why the disorder is persistent, recent studies have suggested that immune complex storage occurs in the cartilage.[24] Indeed, cartilage

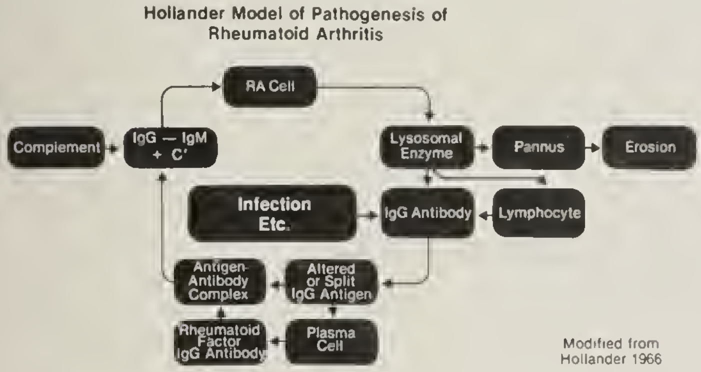
Hollander Model of Pathogenesis of Rheumatoid Arthritis
RA Cell
Complement
IgG — IgM + C'
Lysosomal Enzyme
Pannus
Erosion
Infection Etc.
IgG Antibody
Lymphocyte
Antigen-Antibody Complex
Altered or Split IgG Antigen
Rheumatoid Factor IgG Antibody
Plasma Cell
Modified from Hollander 1966

FIGURE 2
"Rheumatoid Roots" — Current concepts of pathogenesis of rheumatoid arthritis based on concepts elaborated in this article.

removed in the course of joint replacements has shown immunofluorescent staining localized in cartilaginous areas (meniscus, articular cartilage, etc.). In a bovine serum albumin induced immune model of arthritis in the rabbit, studied here and elsewhere, persistent synovitis has been found only in areas contiguous with cartilage storage of immune complexes; the synovium at a distance from these sites is free of the immune arthritis.[24] This may explain why after total joint replacement, patients often have a marked remission in the joint so treated. Synovectomy alone is known to give temporary relief, although as the synovium regenerates over a 1 to 3 year period inflammatory manifestations recur. One may speculate that the removal of the antigen storage sites eliminates, at least for a period, the inflammatory trigger. An ideal regimen would be a substance causing immune complex catharsis from cartilage storage sites, but this has not yet been devised.

Conclusion: We have now moved from the old-fashioned and simple concept of pannus "eating up the joint" in RA to complex interactions among many pathogenetic mechanisms. Some of these are well established, others are still to be conclusively proven. Enumerating these facets is essential if one is to utilize therapy effective for each of the possible mechanisms. Table 1. summarizes the mechanisms we have discussed and the therapeutic possibilities applicable to each. These have been previously enumerated in the text. While Hollander's model is still applicable, the details and new mechanisms elaborated in the past decade complicate the picture. In conclusion we present a more complicated schema of interrelationships in the pathogenesis of RA (Figure 2). This has been entitled "Rheumatoid Roots" because of the similarity to a family tree with many complex interrelationships which are difficult to unravel. Again, the understanding of pathogenesis is requisite to therapeutic research and key to eventually preventing disease.

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Arizona Medicine

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The Science Watch

William Bennett

Lately, surgeons have been hearing a refrain — "Unnecessary surgery. Unnecessary surgery. Unnecessary . . ." — and glimpsing the budget-cutter's knife. Early last November, Hale Champion, now Under Secretary of Health, Education, and Welfare, announced a program through which the government will pay for second opinions on the advisability of surgery. The pilot study is to begin with Medicare recipients in New York and Michigan. Through a related project in Massachusetts, Medicaid patients will also receive financing for second opinions.

The object of Champion's program is to reduce the number of frivolous operations performed on government-subsidized patients. Obviously the program will have an appreciable effect only if surgeons significantly disagree about the need for surgery in certain conditions. And only if Medicare and Medicaid patients are, in fact, being subjected to unwarranted surgery.

The belief is widespread, and probably correct, that Americans experience too much surgery. Every year almost one American in twenty goes into the hospital for an operation. Some of the most common procedures, such as the tonsillectomy for which I was made to see butterflies, and elective hysterectomies, are more and more regarded as justifiable only in rather special circumstances. (Yet tonsillectomy remains the most common surgical procedure in North America.)

It appears to be true that Medicare and Medicaid have contributed to the increase in surgery. Between 1963 and 1970 — the period when Medicare and Medicaid were instituted — the rate of surgical operations rose by fourteen percent. A natural inference to draw from these bare figures would be that the government was subsidizing increased surgery for the indigent and aged. Moreover, an economist might hypothesize that the increase was likely to consist mainly of luxury procedures, operations that were not particularly "necessary" as long as they were relatively costly to the patient. If this reasoning is valid, Medicare and Medicaid patients should be an ideal target for economy measures.

About a month before Champion's announcement, however, an article appearing in The New England Journal of Medicine reported some facts about people on whom surgery is performed. The authors — Claire Bombardier, Victor Fuchs, Lee Lillard, and Kenneth Warner — did not find that the increase in surgery on lower-income and older patients consisted of "unnecessary" procedures. (The authors were rather careful to define "necessity" and to obtain confirmation from a panel of physicians. I think it unlikely that their finding can be dismissed merely as sloppiness of definition, though it does depend on prevailing medical opinion.)

Despite the marked increase between 1963 and 1970 in frequency of operations, the "necessity score" did not budge, even in disadvantaged groups that had come under the government's insurance programs, nor did it vary much among groups with different incomes.

William Bennett, M.D., is science and medicine editor at Harvard University Press and a member of this magazine's editorial advisory board. Harvard© Magazine, Jan.-Feb. 1978. Reprinted with permission. This is an abridged version of original editorial.

The least necessary operations seemed always to be performed on children under the age of nine and on women. Although the authors do not say so, we might guess that tonsillectomies and hysterectomies account for the relatively low necessity scores in these two groups.

H.E.W.'s second-opinion maneuver may help to restrain a few surgeons who flagrantly pay the office rent with tonsillectomies or support a mistress with hysterectomies. That there are enough practitioners of this sort to show up in the Department's statistics I seriously doubt. The new program may also check the enthusiasm of some doctors who operate much more aggressively than their colleagues.

In Vermont, John Wennberg and Alan Gittlesohn were able to demonstrate a marked variation in the frequency of tonsillectomies from one area in the state to another. In one period, 1969-71, the annual rate by area varied from a low of 0.04 percent to a high of 4 percent of children between birth and age 25. When these data were reported to the state's surgeons, those who were at the extremes appeared to respond by adjusting their rates of tonsillectomy toward the state's mean value.

The second-opinion program could have a similar effect simply be exposing surgeons systematically to the opinions of other surgeons, but I doubt that it will. The program depends upon indigent and elderly patients' voluntarily seeking second opinions. I have talked to any number of middle-aged, middle-class, articulate, formally educated people who were reluctant to seek second opinions for fear of offending their primary physician, or who thought it might be unethical, or who simply did not know where to go for another evaluation. Recipients of Medicare and Medicaid hardly seem likely to be less intimidated by their encounters with the medical profession or less inhibited about seeking confirmation for recommended surgery.

Questions of when an operation is "necessary" may go well beyond the matter of effectiveness. Appendectomy, for example, is clearly an effective operation for appendicitis. But because the diagnosis of appendicitis cannot always be made or ruled out with certainty, some "unnecessary" appendectomies are, in fact, necessary. In the United States, at present, about 20 to 30 percent of appendectomies yield organs without demonstrable disease. In Germany the proportion is about 75 percent. Obviously, "necessity" depends only in part on data — cultural values and surgical tradition play an important role.

The strictest measure of "necessity" is the amount of life that patients gain or lose, on average, from a particular course of therapy. This quantity can be expensive and time-consuming to establish, but some sophisticated new methods have improved the available estimates. Results of several such studies are reported in a new book, *Costs, Risks, and Benefits of Surgery*, edited by John Bunker, Benjamin Barnes, and Frederick Mosteller (Oxford, 1977).

Contributors to this volume have studied such operations as elective repair of hernias in men aged 65 or older, elective hysterectomy (usually performed in premenopausal women 40 to 50 years of age), and the removal of gall bladders containing asymptomatic stones. The main question asked in each case was: Does the patient live longer with or without surgery? Their analyses favored a truss over surgical repair for the older hernia patient; removal of the normal, if symptomatic uterus; and either removal of a wait-and-see approach for the stone-filled gall bladder, depending on whether the patient is considered a "good risk" for surgery. But in each case the difference in life expectancy as a result of following the more "favorable" course was *at most* a month or so.

This finding removes some common surgical decisions from the realm of the obvious. Saving lives, the ultimate medical rationale, appears not to be an appropriate justification for the three procedures. But that does not automatically mean they should never be performed. It does, however, shift the grounds upon which a decision can be based. The quality of a patient's life, not brute survival, becomes the paramount concern.

The opinion that counts, when quality of life is at issue, is not the second surgeon's. It is the patient's. To decide whether an operation is necessary, in fact, requires very explicit measurement of the value that a patient places on a breast, a tonsil, or a uterus; on pain; or on wearing a truss for a chronic hernia. Patients will need to learn about such matters and how not to be intimidated by doctors. Doctors must learn how to educate and elicit this third opinion.

The overriding point, as I read the above, is that we must educate the public. Not only in regards to third opinions but in other facets of medical care. We can no longer sit back and dictate. We must help the patient help us! This is a far cay from what we have been doing and it it going to take a reappraisal of our techniques and values. We must go out and do some teaching, both in our offices and in the media. We must bury our fears of self-aggrandizement and present a clear and concise picture to the public through channels which heretofore we have shunned. MBB

Southwest Arthritis Center

Through the Arthritis Act of 1976 the U.S. Congress established a program of fifteen regional arthritis centers throughout the United States, one of which is in Tucson. This program is unique in that it involves a coalition of the University of Arizona College of Medicine, the Southwest Chapter of the Arthritis Foundation and Tucson's private physicians. John Boyer, M.D., is Director of the Center. Of particular importance in the selection of Tucson was the emergency of the U of A's new School of Health Related Professions.

Each designated Center is required under the Arthritis Act to be proficient in research, education and community programs. However, Center grant funding so far has emphasized almost entirely the latter two components, leaving research funding to be accomplished through established channels.

The Southwest Arthritis Center (SAC), as the new program has been designated, has emphasized several projects. Arthritis education has been introduced into the curriculum of the School of Health Related Professions as well as into the nursing program of the several southern Arizona community colleges. A dramatic shift has occurred in arthritis teaching in the undergraduate and graduate curriculum at the College of Medicine through the efforts of Drs. Paula Stillman and Eric Gall. Based on extentive early work by Dr. Stillman in the development of "Programmed Patients," they have trained patients with stable arthritis to offer detailed feedback to students or physicians who perform joint examinations upon them. In this way, each student can instantly correct mistakes and also be advised of some of the more personal and human aspects of doctor-patient relationships. The program has been popular, successful and cost-effective. Also, for the first time, it has been a relatively simple matter to develop performance criteria to determine when residents are eligible to take their specialty boards. Under the leadership of Gail Riggs, M.A., a series of seminars and community programs has been established for advanced education in arthritis for health professionals and for the education of patients themselves and their families.

A particularly novel facet of the SAC program is a study in medical economics, comparing the style and effectiveness of arthritis care in a charity, HMO and a private office setting. Physician time, tests ordered, medicines prescribed and the use of surgery are some of the aspects being studied. This study is being conducted by Josephine Gordon, Ph.D., of the College of Business and Public Administration with major help and cooperation from the Southwest Chapter of the Arthritis Foundation and Tucson's private physicians.

Finally, a major effort at postgraduate medical education is taking place in the offices of private care physicians. A team of arthritis care (TAC) specialists, consisting of a rheumatologist, a physical therapist and a counselor, visit with problem patients in the doctor's own office, offering in-depth consultation. Programmed patients visit the same doctor both before and after this intervention in an effort to assess the effectiveness of arthritis teaching as well as to add a major emphasis on a review of joint examination. Dr. Boyer, of the College of Medicine, James Parsons, M.D., of Tucson's private rheumatology sector, and Beth Ziebell, Ph.D., and Betty Wickersham, R.P.T. of the Arthritis Foundation are responsible for this project.

Nationally, the Arthritis Centers Programs are taking many different forms, adapting to the problems of large cities and special ethnic groups as well as specializing in certain facets of arthritis, such as pediatric rheumatology. In Arizona, the emphasis will continue to be on postgraduate education, since such a large number of health professionals migrate to Arizona without previous interest in the problem of the patient with arthritis, only to find that there is approximately a tenfold increased incidence of arthritis in our state.

Other participants in this cooperative program include Darrell Sabers, Ph.D., Evaluator of the College of Education, and Warren Benson, Ex. Dir. of the Arthritis Foundation, Southern Arizona Chapter.

John T. Boyer, M.D.
Primary Investigator for the
Southwest Arthritis Center
Tucson, Arizona

Louis J. Kettel, M.D.
Dean, College of Medicine
University of Arizona

Auxiliary Highlights

We don't hear too much about turning over a new leaf any more, but surely the traditional philosophy still prevails around new beginnings and January. Perhaps the pages turn too automatically for us these days, stealing our incentive to self evaluate and vow to improve by our own volition; but pages from an old book can still hold fascination and arouse motivation. Just such a book recently resurfaced in the form of Auxiliary records, and turning the leaves of the 20 year old memo pad revealed the continuing nature of basic Auxiliary program even in the wake of heralded new directions.

The old notebook strongly recognized the act of community service as the generator of resulting public relations. Safety concerns related to being a self safe driver, helping the teenage driver, and keeping the drinking driver off the road. The three concerns were paralabeled engineering, education, and enforcement; or urban, suburban, and bourbon!

Familiar headings demanded underlined attention advising constituents toward "be your age" maturity, educating the public, and thumping A.M.A.E.R.F. as a year 'round effort. Projects aimed at solving the problems of the aged (now more becomingly termed aging), sound nutrition, medicine as a career, and freedom of choice.

We were invited to analyse ourselves on seven still pertainent points: adjustability, attitude, maturity, impulse control, purposefulness, self-integrity, and compassion. With actions continuing to speak louder than words, a little self analysis is not yet outdated.

Even an old joke recycled through the notes of two decades ago. You remember the one about the golfer flailing a sand trap ant hill into oblivian except for two ants, one of which was heard to say, "Hazel, if we're going to get out of this, we'd better get on the ball." In some areas we're apparantly still looking for toe holds; but with recycling being fashionable today, we keep seeking new answers to old problems as well as tackling new challanges. So if you think the ladies are "trying", we can only but agree.

Mrs. Melvin W. Phillips
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Correspondence

Central Arizona Health Systems Agency Doings Which May Have Escaped Your Notice

Editor
Arizona Medicine
Dear Sir:

The local health systems agency CAHSA n a determined effort to bring the local nursing homes up to what they thought was a minimum standard of care, they were able to persuade the Legislature to pass legislation in mid 1977 authorizing the agency to perform these inspections using Federal funds under authority supposedly derived from that magnificent umbrella P.L. 93-641. The issue was challenged by the Arizona Associations of Health Care Facilities representing thirty-five long term care facilities statewide. They objected to having these inspections performed by CAHSA using Federal money and probably a bunch of other legal reasons. The HEW regional office in San Francisco on April 3, ordered CAHSA to halt the inspections pending a legal review.

As might be suspected there is already ample State legislation to enable the State Health Department to conduct such inspections and to require that these long term care facilities meet certain standards of diligence in their care of the patients. As we understand it this has never been assiduously followed by the State Health Department using the usual complaint that the Legislature does not appropriate enough money for them to carry on this duty along with all of the others that are assigned to the health authorities on a State level.

It seems to some of us that if the State Medical Association wanted to exert some real leadership in a matter such as this they would exert whatever assistance that they can command in first of all determining whether or not the State Health Department really has enough money to undertake these inspections, or if not to support legislative aid so that this can be undertaken. There are still a few of us around who remember the drive by the late Fred Holmes, Jr. to "clean up the rest home situation" here in Maricopa County and his early demise brought this to a sudden halt.

Furthermore if the County Hospital or the Board of Supervisors who have the governing power allow their patients to be subject to less than adequate care in the many rest homes in which they lodge patients, then that would be another point of understanding to work at.

So as much as you may abhor the CAHSA line in taking up this inspection duty, and they have only been deterred by their own higher authority, so as much as you may abhor it, what has the Profession done locally to remedy these inadequacies in the long term care facilities, and if there are no inadequacies then what have we done to protect them?

Some may recall that the local HSA has made the conflict of interests quite so obtuse that physicians and hospital administrators are almost forbidden, under the local rules and regulations as interpreted by the attorney for CAHSA, it has almost made it mandatory that they don't vote on anything that has to do with medicine.

As reported in the local CAHSA news, the New York interpretation concerning this problem is a bit different. "For example, a hospital administrator can participate in issues that effect hospitals generally even though the resolution of those issues may have a significant effect upon his own institution. Similarly, a physician may vote on issues in which all physicians as a group have an important interest.

"The participation of hospital administrators and physicians in decisions of this kind was clearly intended by Congress when it enacted Public Law 93-641." As I recall the local CAHSA bureaucracy brings into play a State Law which in effect states that no one can serve as a decision maker on a board which lays down rules or regulations etc. which may directly or indirectly affect his business or profession. Now the lawyers have a lot of legalities for this but this was the vomit which was emitted at one time to those of us who sat on the board and I presume it still is.

For example, when the bed plan committee was considering and revising the number and type of beds which CASHA would contemplate authorizing for the next year or so, it was quite alright for physicians and hospital administrators to be heard but those who sat on the board in which these guide lines were finally adopted were forbidden to vote on for approval or disapproval of the committee report because of this "conflict of interest." In effect this is a very subtle method of dis-enfranchisment of the health providers who by law constitute a minority on the board. It is amazing how gullible our business friends become when they serve on a board such as this and exert all kinds of authority and expertise about subjects that they are less than well informed. If the tables were turned and suddenly there was a public law which stated that all industry would be regulated by consumers and that the manufacturers would have only minor representation on the boards which promulgated these regulations and that even though they were represented they couldn't vote, they might quickly understand the dilemma of the health providers. Well in effect that is what has already happened, business at all levels is regulated by the Federal Bureaucracy on which such few if any representatives from the industries which they are regulating, this is part of the unsolved part of big government. Perhaps Mr. Jarvis has the only practical solution, you cannot reason with these people, you cannot ask them to spend less money but you can shut off the money and my guess is that in the great State of California where they are screaming about letting off teachers and firemen and policemen that the pencil pushers in the higher echelons of administration lose very few personnel. The same thing obtains in the Military and Naval circles. When there is a reduction of forces the reduction becomes from the troops on the line, the platoons, companies and battalions and from the seamen who man the ships, not from the bureaucracy in the Pentagon. Example: after WWII the Coast Guard endeavored to have Congress approve something over fifty flag positions, that is fifty admirals and the forced reduction was going to bring the Coastguard overall personnel back very close to pre-war II numbers and as I recall when I served with the Coastguard as a medical officer, prior to WWII there was one flag officer commanding the entire establishment. After WWII they wanted over fifty simply because they had them and they wanted to treat their flag bearing admirals with ease and comfort.

John W. Kennedy, M.D.
(Dry Gulch Jake)

Editor
Arizona Medicine

Dear Sir:

Admittedly we have too many meetings. Some of them however are rewarding. It's hard to know in advance which meetings will be worthwhile and which are like yawnsville.

We have a meeting coming up in February (the 17th to be exact), that in the interest of enlightened self-interest, you won't want to miss. It has to do with our very existance as independent agents and free practitioners. The malpractice problem is of greater significance than the socialization of medicine, because if the malpractice dilemma isn't solved, socialization follows by default, one hundred percent!

What can we do? We can pony up $40 for 7 hours of credit for CME and sit down together to hear some of the Nation's leading authorities on the subject, discuss the situation, and perhaps learn how to stay out of court as defendants.

We have three of the members of the Secretary's Commission on Medical Malpractice coming. Howard Hassard, for many years General Counsel for the California Medical Association; John Linster, head of Employer's Insurance of Wausau, and Dr. George Northup, Editor of the American Journal of Osteopathy and former President of the American Osteopathic Association. Additionally, Dr. Don Harper Mills whose work on the recent Medical Insurance Feasibility Study is of great importance. Dr. Mills is Clinical Professor of Pathology at the University of Southern California and past president of the College of Legal Medicine, and an Advisor to the Commission on Malpractice. Dr. Jack Brooks of M.I.C.A. has some experiences to relate that may curl your hair and will outline "The Anatomy of a Malpractice Suit." Last but certainly not least is Harry Cavanagh, our Confessor, Advisor and Defender, who will have some reasons that have made him wish that he had someone else for a client.

We'll have discussions, questions and answers, we'll cry a lot, but we'll be doing ourselves a favor.

It'll be at Camelback Inn, Saturday, February 17, 1979. Watch for the brochure from Good Samaritan's Continuing Medical Education Committee.

The title of the seminar? "And Then Doctor, Tell the Jury What Happened!"

Sincerely,

Paul B. Jarrett, M.D.
Program Chairman
Department of Pathology, S-4

In Memoriam

Clarence L. Robbins, M.D.
1903 - 1978

Clarence L. Robbins, M.D. died quietly in his home on October 6, 1978. "Chunky" attended Yale College as an undergraduate and obtained his M.D. degree from Yale School of Medicine in 1929. After serving an internship at the New Haven Hospital he joined a small group of house officers at the Desert Sanatorium at Tucson, Arizona. He and several others who were resident physicians at the institution that later became Tucson Medical Center, returned to Tucson and became, in due course, Chiefs of its Medical Staff. After another residency in medicine at the California University Hospital in San Francisco Dr. Robbins returned to Yale where, for the ten years before leaving, he was an Assistant Clinical Professor of Medicine. During World War II "Chunky" was a member of the Yale General Hospital, serving mainly in the Pacific, and achieved the rank of Lieutenant Colonel of the Medical Corps.

In 1946 "Chunky" returned to Tucson and became a member of the Medical Staff of the newly organized Tucson Medical Center. He was President of the Medical Staff at T.M.C. during a trying period and he and a group of devoted physicians and nurses were instrumental in the sound development of the hospital. During his active career "Chunky" was called upon to use his many talents. He served as a President of the Pima County Medical Society, President of the Board of Arizona Blue Cross and he was also President of the Arizona Heart Association and the Tucson VNA. He participated in many national conferences and committees, particularly those dealing with the problems of the aging and the chronically ill. Because of the slow progression of his pulmonary disability Dr. Robbins decided to retire from the private practice of medicine in 1968. Shortly thereafter he began a new career in public health and became a Deupty Director of the Pima County Health Department. Two years later he was made an Associate in Internal Medicine at the University of Arizona School of Medicine and after his retirement from the Pima County Health Department in 1973 he continued to serve as a member of the Board of Directors of Tucson Visiting Nurse Home Health Services. In 1976 Dr. Robbins was the recipient of the Centurion Award of St. Mary's Hospital in Tucson.

Throughout his life "Chunky" retained his gracious courtesy and with each change in his career he left many devoted patients and friends. He is survived by his wife Lucia Allyn Robbins. Diminishing pulmonary function had no dulling effect on his sharp wit nor his articulate speech. Having known "Chunky" is an experience his friends will always treasure.

ArMA
Medical History

The Revolting Revisionist Historian Perspective

Dry Gulch Jake
Squaw Peak Billie

It was bound to happen, but nonetheless it is exasperating. Quite innocently one of us asked a recent RN graduate, university type, what had been said of Florence Nightingale. "Oh", she cheerfully rejoined, "Flo had syphilis." Since we were sure that this was simply an aberrant sampling other recent graduates of the nursing profession were asked the same question and about two out of three came up with the same "syphilis vomit." Pressed as to what else Miss Nightingale may have contributed to the women's lib or nursing education there seemed to be little if any knowledge. Something about she carried a amp in a war and was thought to have been a nurse.

So with this great new generation, the permissive crowd, which has reintroduced syphilis and gonorrhea in epidemic proportion, we have the revisionist, historians who feel that they must bemean and belittle anyone of historic fame. Why they should direct their venom to this brilliant woman who brought their profession, nursing, literally from the gutter to that of respect and knowledge, just why they should wish to do it to Miss Nightingale is beyond the ken of "us squares."

When Miss Nightingale died at the turn of the century (1910) there was over a thousand approved schools of nursing flourishing here in these United States alone. When she went to the Crimea in 1853, not a one existed.

Just as President Lincoln, when told of General Grant's alcoholic propensities allowed well if he could generals to win battles like Grant, he would gladly supply the nectar. So if the present revisionists could discover a pristine leader, an innovative someone to bring nursing care away from the ill equipped nurses aides and place it back into the hands of qualified trained nurses, they are welcome to all of the tickling that the treponema pallida which their cerebral cortex can harbor. Perhaps she could re-discover and re-splendorize bedside nursing, which except for those jewels in special care units, and an occasional ward nurse who has not yet been surrounded by glass and turned into a pencil pusher, some of us would welcome such a saint on the scene.

And while the present faculties of nursing contemplate the blood gasses, chemotherapy, physicians assistants, and all those other exotic goodies of present day hospitals, they might pay passing attention to the fields of medicine which Miss Nightingale enlightened and originated such as:

Bedside nursing;

Hospital construction to make the rooms light and airy and cheerful;

Proper diet care and preparation;

Record keeping, record the observations on signs, symptoms of the patient and the nursing procedures given;

She forced the re-organization of the medical department of the British Army against the bureaucratic odds of gigantic proportions.

"The mortality of the Crimean disaster, 73% in six months from disease alone was the ghastly fruit, not of war, but of the system which controlled the health administration of the British Army." (And we might add also it was the product of the unenlightened physicians who were in charge of it).

"After Miss Nightingale's return from the Crimea she never made a public appearance, never attended a public function, never issued a public statement. "All that she accomplished thereafter was done by goading and tutoring friends and government functionaries." She became a confidante for Queen Victoria and gained leverage over the dilatory government bureaucracy. She had many set-backs and failures and this not infrequently drove her into long periods of melancholy and depression. None of the records of her health or her work make any mention of a leuetic infection and just where this myth arose, except in the pea-brains who now teach non-bedside nursing has yet to be disclosed.

And if any of these great revisionists think she was a prude and not knowledgeable about the facts of life you might consider what she wrote in 1862 about the causes of vice in the army believing they were "moral but not physical." "They are," she wrote, "1. Filthy crowded dwellings. 2. Drunkenness. 3. Ignorance and want of occupation." The way to improve the soldiers' morale was to improve his living conditions. "In civil life you don't expect that every workman who does not marry before he is thirty will become diseased" she wrote in 1861. "In military life you do." Why? Because a workman may have occupation and amusement and consort with honest women. People always say a woman can't know anything about it. It is because I know more about the actual working of the thing than most men, that I cannot hold my tongue." She advanced views with such force that in 1862 she was officially invited to submit a paper, giving her first hand experience in barracks and hospitals.

St. Thomas's Hospital, built in Laur Beth in 1868-71, and became the name for Nurses Training School founded in appreciation of Florence Nightingale's work. The foundation stone was laid by Queen Victoria on May 13, 1868.

Her study of the administration of the army in India and her recommendations for sanitary change in conditions there made her position "in Indian affairs" even more extraordinary than her position at the War Office. "She had never been to India, she never did go to India, yet she was considered an expert on India and consulted on the affairs by men who lived there all of ther working lives. She possessed prodigious powers of absorbing, retaining, and marshalling masses of facts, and when she completed her task a whole vast teeming country laid before her mind's eye like a map."

Three years after she returned from the Crimea, at constant urging, she had worked out the plans for a nursing school.

One of her biographers describes the selection of the matron. "Mrs. Wardroper, matron of St. Thomas's Hospital, a gentle woman by birth, had been left a widow at the age of 42 and had taken up nursing. Miss Nightingale wrote, "Her force of character was extraordinary, and she learned from intuition." She was appointed matron of St. Thomas in 1853 and held the post of Superintendent of the Nightingale Training School for 27 years and the greate part of the success of the school wa due to energy and determination." In May 1910 and Jubilee of the founding of the Nightingale Training School there were over one thousand training schools for nurses in the United States alone.

Syphilis, indeed.

REFERENCES

History of Nursing by M. Adelaide Nutting, R.N., and Lavinial Dock, R.N. Vol. II G.P. Putnam's Son, London 1907.

Florence Nightingale 1820-1910 by Cecil Woodham-Smith, McGraw Hill, New York, 1951.

The Invasion of the Crimea by R. Kinglake, London 1880, Vol. VI, P. 409.

ArMA Reports

HE MINUTES APPEARING IN THIS SECTION HAVE EEN EDITED TO CONSERVE SPACE A COMPLETE OPY OF THE MINUTES OF ANY MEETING WILL BE AILED TO ANY MEMBER REQUESTING THEM.

MEDICAL EDUCATION COMMITTEE

Meeting of the Medical Education Committee the Arizona Medical Association, Inc., held Thursday, September 28, 1978, at 810 West ethany Home Road, Phoenix, convened at 00 P.M. Robert E. T. Stark, M.D., Chair- an, presiding.

SECTION REPORTS

ection on Accreditation: - William F. Sheeley, .D., Chairman.

In the absence of the Chairman, Harry F. enhardt, M. D. reported on activities of the ection. He indicated that the Section had pproved the recommendations of survey teams ho had visited Desert Samaritan Hospital, hoenix Indian Medical Center, Scottsdale emorial Hospital and Mesa Lutheran Hos- ital. The Committee approved accreditation of e four hospitals by the following actions:

IT WAS MOVED AND CARRIED TO PPROVE CONTINUED FULL ACCREDI- ATION OF DESERT SAMARITAN HOS- ITAL FOR CONTINUING MEDICAL EDU- ATION FOR A PERIOD OF FOUR YEARS.

IT WAS MOVED AND CARRIED TO PPROVE CONTINUED FULL ACCREDI- ATION OF PHOENIX INDIAN MEDICAL ENTER FOR CONTINUING MEDICAL DUCATION FOR A PERIOD OF FOUR EARS.

IF WAS MOVED AND CARRIED TO RANT FULL ACCREDITATION OF COTTSDALE MEMORIAL HOSPITAL FOR ONTINUING MEDICAL EDUCATION OR A PERIOD OF TWO YEARS.

IT WAS MOVED AND CARRIED TO RANT FULL ACCREDITATION OF MESA UTHERAN HOSPITAL FOR CONTINUING EDICAL EDUCATION FOR A PERIOD OF WO YEARS.

Resignation of Harry F. Lenhardt M.D.

Doctor Lenhardt announced he will no longer e Director of Medical Education at Mari- opa County General Hospital, and is there- ore resigning from the Medical Education ommittee. He introduced Steven J. Schaffner, .D., who is replacing him at the hospital. octor Schaffner was invited to attend meet- ngs of the committee in the same capacity as octor Lenhardt has in past years. Doctor enhardt was thanked for his years of service to he Committee.

ection on Certification: - Ashton B. Taylor, .D., Chairman.

Doctor Taylor reported that the Section had onsidered requests for extensions or other pecial consideration from several physicians ho were due to report in 1977, and who have ot as yet met their CME requirements. He ommented that many are the same ones the Section has given consideration to in the past, and that the Section Members feel that further extensions cannot be granted. Letters will be written informing them of that fact, and pointing out that ArMA Membership is suspended for one year before actually being dropped, and therefore they do have until the end of 1978, to complete the requirement and retain their membership, but otherwise they will be dropped at that time. In a few cases where a disabling illness prevents attendance at meetings, doctors have been given the option of submitting written reviews of reading material in lieu of active CME participation. One or two have availed themselves of this opportunity.

Doctor Taylor reported that there are approximately 300 physicians who have not yet completed their CME requirements for the 3-year period ending December 31, 1978.

Special Circumstances:

There was brief discussion of the possibility of offering some other option to physicians in very limited practice who cannot attend meetings, but are performing a valuable service by their continued practice. It was suggested that the Board of Medical Examiners might be asked to give consideration to this so that those physicians would not lose their license to practice medicine.

Section on Requirements: - Albert G. Wagner, M.D., Chairman

Doctor Wagner reported that the Section, since the last meeting, had revised the Guidelines for the ArMA Certificate in Continuing Medical Education in order to bring our criteria as closely as possible into conformance with the criteria for the AMA/Physician's Recognition Award.

Doctor Wagner reported that the Section has also developed guidelines for Co-sponsorship by accredited organizations. Portions of materials from several other state associations were incorporated into our guidelines. Doctor Wagner reviewed the background, explaining that ArMA can no longer approve individual programs because we wish to retain our reciprocity with the Physician's Recognition Award. We are instead encouraging that non-accredited presentors of CME Programs seek Co-sponsorship.

An accredited organization, in order to Co-sponsor, must be represented by an individual in their organization who will act as liaison and report to the sponsoring organization on development of the program. He suggested that specialty representatives from the Medical Education Committee be utilized in cases where we might be asked to Co-sponsor Programs of a specialty society. Members are asked to cooperate if asked to serve in this capacity.

ACCREDITATION PROCESS AND LCCME

National Council of State Chairman of Continuing Medical Education (NCSCCME): Melvin D. Small, M.D.

Letter of August 30, 1978, asking for support of Doctor Small as a Nominee for the Liaison Committee on Continuing Medical Education (LCCME) was received for information

Liaison Committee on Continuing Medical Education:

The Committee had been provided several documents to review, including (1) "Proposed Changes — (in) — Accreditation" by the LCCME dated June, 1978, (2) Memorandum dated August 11, 1978 from the LCCME enclosing their revised report form and (3) Report dated June 13, 1978, from Doctor Stark to ArMA Delegates to the AMA.

Doctor Stark briefly reviewed the history of state association involvement in accreditation, and stated that we were originally designated as an accrediting organization; this authority delegated by AMA, who approved the accreditation actions taken by our Medical Education Committee. Without prior notice this designation was suddenly changed, in 1976, to "A Survey for Accreditation Program," just prior to the LCCME assuming the role in accreditation previously held by the AMA. Doctor Stark described the subsequent dissatisfaction of many state associations with the change, and the formation of the NCSCCME as a result. California Medical Association's refusal to acknowledge the LCCME's role as sole accrediting agency was reviewed.

Doctor Stark pointed out that it is his feeling, as well as that of the California Medical Association, and others involved in the NCSCCME, that there should be a national umbrella organization who would approve the state associations for accreditation of intra-state institutions and organizations (as was originally the arrangement with the AMA) and that the national organization, whatever it might be, would review state association's programs periodically.

LCCME requires that reports of surveys be summarized in a form they have developed, and will accept no other type of reporting. Reports of state association accreditation actions go first to a review committee which decides whether or not the accreditation recommendation will be accepted, (often returning for further information,) and if approved, it is then forwarded to the LCCME itself, who must pass on it. The entire process can take six to twelve months, and results in considerable inconvenience at the state level.

Doctor Stark feels that state associations do have the expertise at the state level to make determinations regarding CME Programs of local institutions and organizations, although the inference is that the LCCME does not feel this is the case.

Considerable discussion ensued, with observations from many committee members, resulting in the following action:

IT WAS MOVED AND CARRIED THAT THE CONSENSUS OF THE COMMITTEE IS THAT WE STILL LOOK UPON OURSELVES AS AN ACCREDITING BODY AND ARE NOT WILLING TO RELINQUISH THAT RIGHT TO THE LIAISON COMMITTEE ON CONTINUING MEDICAL EDUCATION, AND THAT WE WILL CONTINUE TO SUBMIT TO THE LIAISON COMMITTEE ON CONTINUING MEDICAL EDUCATION, COPIES OF THE REPORTS OF OUR SURVEY TEAMS, AND MINUTES OF THE MEDICAL EDUCATION COMMITTEE MEETINGS CONCERNING ACCREDITATION ACTIONS.

CME CONFERENCE

Doctor Stark called attention to the 6th Annual Conference on CME to be held in Chicago, October 3-5, 1978. The NCSCCME will be meeting then also, and both Doctor Stark and Misty Coumbe will attend that meeting. Mrs. Coumbe will attend the Conference.

CMSS CONFERENCE

Letter dated September 13, 1978, announcing a meeting on CME accreditation in January, 1979, was received for information. No one present expressed an interest in attending.

For nonnarcoti

Yesterday's folk remedies from the Southwest

An old Pueblo remedy—corn-smut decoctions

Traditional Mexican therapy—plantain tea

19th century Pioneer's relief—rice—parched, then boiled

AMA/PRA

It was reported that the ArMA Certificate has again been approved by the Advisory Committee on the Physician's Recognition Award for reciprocity. The AMA accepts our lists of physicians who have received the ArMA Certificate, and issues the PRA on the basis of those lists. Letter from Clarke Mangun, M.D. of AMA, referring to ArMA's "splendid CME Program," received for information.

BOARD OF MEDICAL EXAMINERS

Draft of proposed amendments to the Medical Practice Act pertaining to CME was reviewed. BOMEX seeks to clarify the CME requirement for licensure.

It was reported that BOMEX accepts our lists of physicians holding current ArMA Certificates as sufficient proof for the CME licensure requirement.

CALENDAR OF CATEGORY I PROGRAMS

Proposal to include a calendar of Category I Programs within Arizona, with mailing of **Medical Memos** was reviewed, and approved by the Committee.

FLINN FOUNDATION GRANT

It was reported that the Academy of Medical Sciences of Maricopa County has received a grant from the Flinn Foundation for a "Continuing Medical Education Project" which has a number of objectives concerning Continuing Medical Education in Central and Northern Arizona.

PROFESSIONAL COMMITTEE

Meeting of the Professional Committee of the Arizona Medical Association, Inc., held at 810 West Bethany Home Road, Phoenix, Arizona, on Tuesday, October 31, 1978, convened at 6:40 p.m., Joseph W. Hanss, Jr., M.D., Chairman, presiding.

ADVISOR TO AUXILIARY

Arizona Medical Association Auxiliary Fall Conference

John T. Clymer, M.D., Advisor to the Auxiliary, reported on the Arizona Medical Association Auxiliary Fall Conference which was held September 27-28 at the ArMA headquarters offices in Phoenix. Fifty-five members attended this conference which was open to the entire Auxiliary. This was the first time the Auxiliary had attempted an overnight conference and evaluations were overwhelmingly in favor of repeating the format in 1979. There was an enthusiastic response to the Conference itself; members found the speakers and discussions helpful.

Immunization Program

A letter to Richard L. Dexter, M.D., President, dated October 26, 1978, from the Pima Council to Immunize Children, endorsed by the ArMA Auxiliary, relative to a mass immunization campaign was introduced. The Council and Auxiliary request a grant of $4500 or $5000 from ArMA as additional funding of this program and asked for endorsement of this endeavor by the Professional Committee. It was noted that the Board of Directors had "wholeheartedly endorsed" the project during meeting held July 15, 1978.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THE ENDORSEMENT OF FINANCIAL SUPPORT FOR THE CONTINUATION OF THE PIMA COUNCIL TO IMMUNIZE ARIZONA'S CHILDREN PROGRAM.

SECTION ON AGING AND GENERAL MEDICINE

Richard S. Armstrong, M.D., Chairman, Tucson Medical Center, Human Research Committee, requests the Association consider a "policy position for criteria of death for the personal and legal protection of patient, family, medical staff, and institution." Dr. Armstrong presented a "definition of death" developed by their committee and approved by the Tucson Medical Center for consideration. Robert L. Hagan, M.D. informed the Committee that he has reviewed the request with members of the legal profession as well as other physicians with the ultimate goal of introduction into the legislature a bill embodying such a policy and its passage into law. He is presently collecting information and reports to bring before the Professional Committee for its endorsement at the next meeting. RECEIVED FOR INFORMATION ONLY.

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As nonnarcotic as these folk remedies of yesterday, Cantil is a logical clinical choice in the adjunctive management of diarrhea* today.

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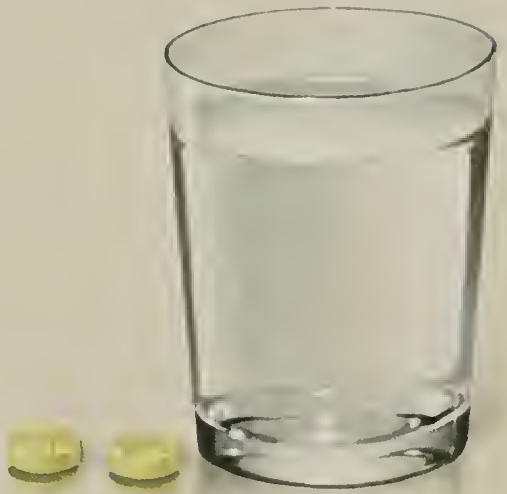

Merrell

*This drug has been classified as "possibly" effective as an adjunct in the treatment of diarrhea

†See Contraindications, Precautions, Warnings, and Adverse Reactions.

See prescribing information on the following page

SECTION ON ATHLETIC MEDICINE

Sports Medicine Symposium

In the absence of Dr. Brainard, Chairman of he Section, it was announced the planning for he 5th Annual Sports Medicine Symposium was well under way. It is anticipated that in excess of 500 physicians, coaches, athletic directors, students, trainers, etc. will attend this symposium at the Adams Hotel on January 20, 1979. RECEIVED FOR INFORMATION ONLY.

Certified Athletic Trainers

At the request of the Professional Committee during a previous meeting, the Board of Directors endorsed the concept of Certified Athletic Trainers in all Arizona schools and actively support the development of programs leading to the training of Certified Athletic Trainers in Arizona Universities. It was suggested that the Chairman of the Section on Athletic Medicine inform the Professional Committee at its next meeting whether ArMA should support mandating this action in law.

SECTION ON DISASTER MEDICINE & EMERGENCY CARE

Emergency Medical Services

Willard R. Van Nostrand, M.D., by letter, submitted a report of the recent activities of the Section on Emergency Care. He noted that Dr. Michael Krentz, President of Arizona Chapter of ACEP, announced the designation of Arizona ACEP to contract with the Department of Health Services to standardize testing procedures and exams for Intermediate EMT's and Emergency Paramedics in Arizona. This program is now underway and will ensure fair, reproducable and educational testing procedures and exams for IEMT's and Paramedics in Arizona. The Section on Emergency Care submitted suggestions for criteria to be used by the Department of Health Services, as per HB 2337, to aid Dr. Suzanne Dandoy define the job description for the Medical Director for the D.H.S. The Section offered its full support to Dr. Donald Kunkel and his Toxicology Symposium which over 200 people attended last month. Many noted speakers in toxicology came to Arizona for this seminar. This Section has also offered its support to a cardiology symposium to be held in Scottsdale in December. Dr. Van Nostrand also reported that four members of the Arizona Chapter of Emergency Physicians have been selected for the ArMA Underwriting Review and Claims Review Committee representing emergency physicians. RECEIVED FOR INFORMATION ONLY.

Management of Radiation Accidents

Willard R. Van Nostrand, M.D. reported on his and Charles E. Harter, M.D.'s experiences in Oak Ridge, Tennessee, last month at a two day symposium on Management of Radiation Accidents by Emergency Personnel. A one-day symposium on this subject will be presented in Phoenix this winter for continuing education. RECEIVED FOR INFORMATION ONLY.

Advanced Cardiac Life Support

Dr. Van Nostrand informed us that a goal of the Section on Disaster Medicine, at the beginning of the year, was to offer full support to programs designed to train 400 (approx.) in Advanced Cardiac Life Support during the year. It appears that this goal will be met. RECEIVED FOR INFORMATION ONLY.

Emergency Room Centers

The establishment of Emergency Room Centers around the state was briefly discussed. Concern was expressed that Emergency Room Centers were being established without appropriate criteria for their development. It was suggested that the Chairman of the Section on Emergency Care be asked to develop appropriate criteria for the establishment of Emergency Room Centers and report to the Committee during its next meeting.

SECTION ON POISON CONTROL

Regional Poison Control Center

The Committee reviewed a proposal by Albert L. Picchioni, PH.D., Director, Arizona Poisoning Control Information Center, for a Regional Poison Control Center program by the state of Arizona. Dr. Picchioni's letter informs us that our present poison control system, established some 20 years ago, may need reevaluation and they ask the support of the Association. As State Coordinator of Poison Control Centers, Dr. Picchioni formulated a

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Brief Summary

INDICATIONS: Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows

"Effective" Cantil is indicated for use as adjunctive therapy in the treatment of peptic ulcer

"Probably" effective Cantil is indicated for use as adjunctive therapy in the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis, acute enterocolitis and functional gastrointestinal disorders) and in neurogenic bowel disturbances (including the splenic flexure syndrome and neurogenic colon)

"Possibly" effective Cantil is indicated as an adjunct in the treatment of diverticulitis and mild ulcerative colitis Cantil is also indicated as an adjunct in the treatment of diarrheas i e , loose stools, functional diarrheas, post-gastrectomy diarrheas (post-gastrectomy syndrome, dumping syndrome), drug induced diarrheas, acute enteritis intestinal viral infection, colitis, ileocolitis and diarrheas with ileostomies and ileoanal anastomoses

To be effective the dosage of Cantil must be titrated to the individual patient's needs

Final classification of the less-than-effective indications requires further investigation

IT SHOULD BE NOTED AT THIS POINT IN TIME THAT THERE IS A LACK OF CONCURRENCE AS TO THE VALUE OF ANTICHOLINERGICS IN THE TREATMENT OF GASTRIC ULCER

IT HAS NOT BEEN SHOWN CONCLUSIVELY WHETHER ANTICHOLINERGIC DRUGS AID IN THE HEALING OF A PEPTIC ULCER, DECREASE THE RATE OF RECURRENCES OR PREVENT COMPLICATION

THESE FUNCTIONAL GASTROINTESTINAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS, ETC

CONTRAINDICATIONS: 1. In glaucoma (particularly narrow-angle) 2 In obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy) 3 In obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis, etc) 4 In paralytic ileus 5. In intestinal atony of the elderly or debilitated patient 6 In severe ulcerative colitis and toxic megacolon complicating ulcerative colitis 7 In acute hemorrhage where the cardiovascular status is unstable 8 In myasthenia gravis
WARNINGS: 1 An early symptom of incomplete intestinal obstruction especially in patients with ileostomy or colostomy, may be diarrhea Treatment with mepenzolate bromide in this instance would be inappropriate and possibly harmful 2 Heat prostration (fever and heat stroke due to decreased sweating) may occur with use of this drug in the presence of high environmental temperature 3 The patient should be warned not to engage in activities requiring mental alertness such as operating machinery or driving a motor vehicle if drowsiness or blurred vision occurs 4 Since the safety of this drug in pregnancy has not been established, use of this drug in such patients requires that the potential benefits of the drug be weighed against possible hazards to the mother and child
PRECAUTIONS: Cantil should be used with caution in patients in which the anticholinergic effects might produce adverse effects, such as in open-angle glaucoma (contraindicated in narrow-angle), autonomic neuropathy, non-obstructing prostatic hypertrophy and hiatal hernia associated with reflux esophagitis In the treatment of gastric ulcer the use of anticholinergic drugs may produce a delay in gastric emptying time and may complicate such therapy (antral stasis) In ulcerative colitis large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon Use with caution in patients with hepatic or renal disease Do not rely on the use of this drug in the presence of complications of biliary tract disease Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate Use with caution in patients with hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias and hypertension With overdosage, a curare-like action may occur
ADVERSE REACTIONS: Anticholinergic drugs produce certain effects which may be physiologic or toxic depending upon the individual patient's response The physician must delineate these Adverse reactions may include dryness of the mouth, urinary hesitancy and retention, blurred vision and tachycardia, palpitations, mydriasis, dilation of the pupil, cycloplegia, increased ocular tension, loss of taste, headaches, nervousness, drowsiness, weakness, dizziness, insomnia, nausea, vomiting, impotency, suppression of lactation, constipation, bloated feeling, severe allergic reaction or drug idiosyncrasies, including anaphylaxis, urticaria and other dermal manifestations, some degree of mental confusion and or excitement especially in elderly persons Decreased sweating is another adverse reaction that may occur It should be noteo that adrenergic innervation of the eccrine sweat glands on the palms and soles make complete control of sweating impossible An end point of complete anhidrosis cannot occur because large doses of drug would be required and this would produce severe side effects of parasympathetic paralysis
DOSAGE AND ADMINISTRATION: Cantil Tablets: Usual Adult Dose One or 2 tablets three times a day preferably with meals and 1 or 2 tablets at bedtime Begin with the lower dosage when possible and adjust subsequently according to the patient's response
Cantil Liquid: Usual Adult Dose One or 2 teaspoonfuls three times a day preferably with meals and 1 or 2 teaspoonfuls at bedtime As with the tablets, begin with the lower dosage when possible and adjust subsequently according to the patient's response
DRUG INTERACTIONS: Concomitant administration of anticholinergic drugs and any other drugs which would increase the anticholinergic effects of Cantil is to be avoided
MANAGEMENT OF OVERDOSAGE: With overdosage a curare-like action may occur Symptomatic treatment of overdosage is directed to the anticholinergic effects of the drug Severe intoxication with oral overdosage of Cantil is unlikely, since, being a quaternary anticholinergic, passage across the blood brain barrier is not known to occur If severe symptoms do occur, gastric lavage should be instituted promptly Physostigmine or other reversible anticholinesterases may be necessary Symptomatic treatment should also be instituted.

(Revised January 1975)

Merrell

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proposed plan for a Regional Poison Control Center for Arizona in which the center would be located at the University of Arizona Health Sciences Center with sub-regional centers located in Phoenix, Flagstaff, and Yuma. A copy of the entire proposal is on file. Helen Johnson, M.D., Chairman of the Section on Poison Control, reported through Mr. Barnett her complete support of the concept and recommends that the Professional Committee's wholehearted endorsement. She further informs the Committee that the Arizona Chapter of American Pediatric Society as well as the Pima County Chapter endorsed the concept. There was considerable discussion.

IT WAS MOVED AND CARRIED TO TABLE THE ENDORSEMENT OF A REGIONAL POISON CONTROL CENTER PENDING A REPORT BY THE CHAIRMAN OF THE SECTION ON POISON CONTROL.

SECTION ON PUBLIC HEALTH

Blood Pressure Computers

The Committee reviewed material on Hypertension Hot Lines and Blood Pressure Computers by Arizona Medical Services. There was a discussion on the accuracy of these computers and the problems which could result from false readings. RECEIVED FOR INFORMATION ONLY.

SECTION ON REHABILITATION MEDICINE

The Committee was informed of the resignation of George Spendlove, M.D. from the Professional Committee and Chairmanship of the Section On Rehabilitation Medicine.

IT WAS MOVED AND CARRIED THAT A LETTER BE SENT TO DR. SPENDLOVE THANKING HIM FOR HIS FAITHFUL ATTENDANCE AT PAST MEETINGS OF THE PROFESSIONAL COMMITTEE AND FOR CHAIRING THE SECTION ON REHABILITATION MEDICINE.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE PRESIDENT AND THE BOARD OF DIRECTORS THE APPOINTMENT OF CLARENCE LAING, M.D. TO THE PROFESSIONAL COMMITTEE AND CHAIRMANSHIP OF THE SECTION ON REHABILITATION MEDICINE, PENDING HIS ACCEPTANCE.

Myotonia Association

The Committee reviewed a letter from James P. Griffin relative to the establishment of a Myotonia Association. The Chairman of this Section will be asked to review this situation and submit a report to the Committee.

SECTION ON SAFETY

Dr. Hanss announced that there is not a Chairman of the Section on Safety. It was recommended that consideration be given to consolidating the Section on Safety with the Sections On Disaster Medicine and Emergency Care. Should it be determined that the section on Safety continue as a standing Section of the Professional Committee, that Charles W. Pullen, M.D. and Hugh C. Thompson, M.D. be considered for appointment by the President.

OTHER BUSINESS

Health Education

Warren L. Niccum, Arizona Chapter Pediatrics Society Chairman on School Health Committee and Handicap Committee reported on their activities. The Arizona Red Cross has a steering committee which is in the process of developing evaluation programs to determine the state of health of Arizona youth. He nformed us that in lieu of a state program of ealth education, an evaluation program may be eeded in each school district before appropriate health education can be implemented. This oluntary approach may prove to be very vorthwhile. Dr. Hanss expressed the need for a ection on Health Education within the Professional Committee to keep abreast of this ndeavor and for official Association input.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT A SECTION ON HEALTH EDUCATION BE ESTABLISHED WITHIN THE PROFESSIONAL COMMITTEE AND THAT A CHAIRMAN BE APPOINTED.

FINANCE COMMITTEE

The meeting of the Finance Committee of the Arizona Medical Association, held at 810 W. Bethany Home Road, Phoenix, Arizona, on Saturday, October 21, 1978, convened at 10:08 a.m., Neopito L. Robles, M.D., Treasurer and Chairman, presiding.

MARICOPA COUNTY MEDICAL SOCIETY'S ArMA BUDGET REVIEW COMMITTEE REPORT

The report submitted by Earl Baker, M.D., as Chairman of the Maricopa County Medical Society's ArMA Budget Review Committee, dated September 21, 1978, was reviewed by the committee in its entirety and dealt with the six specific recommendations contained therein as follows:

A. *That the Arizona Medical Association consider changing its budgeting procedures to allow for effective implementation of zero-based budgeting.*

1. *That each Committee chairman be required to submit written evaluations of performance and its projected programs with the submission of its budget and that each such budget shall adhere to zero-based justification.*
2. *That the budgeting process be done so as to involve the Finance Committee and the Board of Directors and the Executive Committee in the budget decisions prior to its completion and submission to the House of Delegates, and that the President-Elect and the succeeding year's Committee chairmen participate in these budget procedures.*
3. *That the Finance Committee meet at least on a quarterly basis with in depth review of the budget as above (2) immediately prior to the House of Delegates' annual meeting.*

The problems of applying the classic zero-based budgeting process to the committee portion of the ArMA budget was discussed. It was pointed out that the committee chairmen are apointed after the budget for the year has been adopted, making it difficult to get real participation in the budget preparation on a timely basis from the chairmen. This timing is dictated by the requirement that the bylaws mandate that the House of Delegates approve the budget. The House traditionally meets in April and is approving a budget that will not go into effect for eight months. The lead time is even greater as, in order for the budget to be prepared for the House, it must be developed by the Finance Committee in January for Board of Directors approval in February in order to be ready for the House in April.

IT WAS MOVED AND CARRIED THAT MR. ROBINSON PREPARE A PROGRAM ESTABLISHING A WORKABLE TIME FRAME WITHIN WHICH THE CHAIRMEN OF ALL COMMITTEES, SUBSEQUENT TO THEIR APPOINTMENT IN APRIL, COULD MEET WITH THE FINANCE COMMITTEE IN AN EFFORT TO MORE FULLY EVALUATE AND ASCERTAIN THE BUDGET NEEDS FOR THE COMING YEAR; AND THAT SUCH PROGRAM, WHEN COMPLETED, BE SUBMITTED TO THE COMMITTEE FOR REVIEW PRIOR TO ITS RECOMMENDATION TO THE BOARD OF DIRECTORS FOR ACTION.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT IT BE CHARGED TO PASS ON ANY BUDGETARY REVISIONS AT ITS DECEMBER MEETING FOR THE FISCAL YEAR APPROACHING, BASED UPON INFORMATION SUPPLIED BY COMMITTEE CHAIRMEN, THE FINANCE COMMITTEE AND THE EXECUTIVE COMMITTEE.

It was noted that recommendation A-2 is already in effect and has been for a number of years.

With regard to item A-3, the Chairman indicated that he plans on frequent meetings of the committee. It was agreed that future meetings would be held at the discretion and call of the Chairman.

B. *That the Finance Committee members from Maricopa County be urged to attend more regularly.*

It was agreed that this recommendation could best be implemented by those members of the committee from Maricopa County.

C. *That a plan be developed and implemented which will assure greater advertising revenue for Arizona Medicine. Mr. Mitten has volunteered to serve as a consultant for this problem.*

It was reported that steps to implement this recommendation have already been taken by arranging for Ms. Bruner to work full-time, instead of part-time. Arrangements will soon be made to take advantage of Mr. Mitten's offer to consult in the development of this program.

D. *That a greater emphasis be given to other income producing modes including realistic building rentals, printing, special specialty society services, etc.*

Mr. Robinson reported that the upcoming lease with BOMEX calls for an increase that will place the rental of that space on a very competitive basis with other rentals in the area. He also stated that new equipment is being obtained for the printing department and the journal, which will reduce costs and broaden the scope of the printing department. The services to specialty societies has grown over the past few years and should continue to do so gradually. It was pointed out that the charges made to the specialty societies is calculated to have the revenue cover the expense - a break-even basis.

E. *That additional efforts be made to work more actively with component medical societies in planning and implementing service programs, such as shared cost of printing, including journals, accounting and computer, legislative lobbying and public relations and consideration of possible state wide utilization where feasible of the Maricopa County Bureau of Medical Economics.*

The committee wholeheartedly agreed with this recommendation and determined to pursue ways in which these ideas could be developed and implemented. Mr. Robinson pointed out that efforts have been started to develop more comprehensive high quality insurance service programs as a membership benefit. He also stated that ArMA would be happy to bid on printing jobs from the various societies.

F. *That CME processing be assumed by BOMEX.*

This item was discussed briefly, but it was determined not to take action at this time. The Association's policy regarding CME activities rests with the Medical Education Committee and the House of Delegates, with many ramifications to be considered in addition to the cost involved in processing the applications.

MATERNAL & CHILD HEALTH CARE COMMITTEE

The meeting of the Maternal & Child Health Care Committee of the Arizona Medical Association, Inc. held at 810 W. Bethany Home Road, Phoenix, Arizona on Saturday, October 21, 1978, convened at 12:55 p.m., William C. Scott, M.D., Chairman, presiding.

BOARD OF REGENTS POLICY RE: BIRTH CONTROL

Board of Directors action of 4/25/78. RECEIVED.

Lisa Moore letter of 9/25/78. RECEIVED - NO ACTION REQUIRED.

SECTION ON PERINATAL - CYTOGENETICS

Minutes of 3/29/78 meeting. RECEIVED.
Memorandum of 5/3/78. RECEIVED.
Minutes of 7/26/78. RECEIVED.

Current Status

In Dr. Daily's absence, Dr. Harlan Giles briefly reported on each item received for information. Dr. Giles reported that Arizona, in a joint effort with New Mexico, had recently sought a grant from the NICHD, which had been turned down. He also advised that physicians from the Western states would be meeting in Denver next month to discuss genetics resources and the possibilities of establishing greater cytogenetic services throughout the area, following which meeting Dr. Giles would be better informed to present a report to this committee which might include a request for some participation by the committee on behalf of this effort.

HOME DELIVERY BY LAY MIDWIVES

Phoenix Obstetrical & Gynecological Society Letter of 4/24/78

Dr. Moore discussed the contents of the Phoenix OB/GYN Society letter of 4/24/78 and submitted for review by the committee a suggested form for use by hospitals in the reporting of injuries resulting from home delivery and stressed the feelings of the Society that a task force be formed to evaluate the trend for home delivery in the State of Arizona. Following a lengthy discussion on the issue as well as the formation of another committee or any use of the suggested form, it was agreed that Dr. Scott and Dr. Moore would check into the legal ramifications of the use of any such form, as well as possible alternatives to a task force committee, and present to this committee a more tailored package of what actions, if any, should be taken at the present time.

Newspaper Ad re: Midwifery. RECEIVED.

Arizona Public Health Association letter of 6/1/78. RECEIVED.

Arizona Nurses' Association letter of 5/4/78. RECEIVED.

REQUEST FOR GRANT PROPOSAL

Letter of Frederic Baum, M.D., dated October 6, 1978. RECEIVED.

In Dr. Baum's absence, Harold Gabel, M.D. briefly advised the committee on the importance of the grant that was being sought to improve the outcome of pregnancy and that he felt it would be most beneficial to have as many from the committee as possible be present at the site visit scheduled for November 2 and 3, 1978. No further action was required by the committee.

PLANNED PARENTHOOD REQUEST FOR ENDORSEMENT

All responses to the committee's earlier request for comment on the document entitled "Planned Births, The Future of the American Family and the Quality of American Life," were received and discussed by the committee.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT IT TAKE NO ACTION ON THE REQUEST OF PLANNED PARENTHOOD FOR ENDORSEMENT OF THE DOCUMENT ENTITLED "PLANNED BIRTHS, THE FUTURE OF THE AMERICAN FAMILY AND THE QUALITY OF AMERICAN LIFE."

CORRESPONDENCE

Resignation of L. Rex Ehling, M.D.

IT WAS MOVED AND CARRIED TO ACCEPT THE RESIGNATION OF L. REX EHLING, M.D. AND THAT SUCH ACCEPTANCE TOGETHER WITH AN EXPRESSION OF APPRECIATION AND REGRET BE CONVEYED TO DR. EHLING BY LETTER.

Unfair Sex Descrimination In Issuing Insurance

Department of Insurance rule R4-14-209. RECEIVED.

OTHER BUSINESS

Task Force on Alternative Birthing Practices

Following a presentation by Dr. Moore regarding his attendance at the meeting of the Task Force on Alternative Birthing Practices and a discussion by the committee, it was determined that Dr. Scott, as chairman of this committee, should contact and discuss with Dr. Suzanne Dandoy of the Arizona Department of Health Services the contemplated use of any findings or report of the Task Force and report back to the committee the results of such discussion.

Scientific Assembly Committee

Dr. Scott relayed to the committee a recent request he had received as president of the Arizona OB/GYN Society to send a representative to a December 9th meeting of that committee at which would be discussed greater participation by the several societies in the annual meetings of the Association, and in particular, the 1980 Annual Meeting. It was determined that Harold Gabel, M.D. would act as the representative of the Arizona OB/GYN Society at such meeting.

Reporting of Maternal Deaths

Dr. Susong advised the committee that following a request of Dr. Suzanne Dandoy he had been advised that there was presently no statute requiring the reporting of maternal deaths within the state. Following a discussion by the committee,

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE LEGISLATIVE COMMITTEE THAT A BILL REQUIRING REPORTING OF MATERNAL DEATHS BY ALL HOSPITALS THROUGHOUT THE STATE BE PREPARED AND SUBMITTED TO THE LEGISLATURE DURING THE 1979 SESSION.

PHYSICIAN REHABILITATION COMMITTEE

The meeting of the Physician Rehabilitation Committee of the Arizona Medical Association, Inc., held at 810 West Bethany Home Road, Phoenix, Arizona, on Wednesday, November 8, 1978, a quorum being present, convened at 6:41 p.m., Thomas E. Bittker, M.D., Chairman, presiding.

BOARD OF MEDICAL EXAMINERS

Dr. Bittker briefly reported to the committee on a meeting of the Board of Medical Examiners held on September 9, 1978, which he as Chairman of this committee attended, and presented for discussion the request of BOMEX that the physicians on this committee, together with other physicians in the community, serve as resource people to investigate problems relating to impaired physicians reported to BOMEX.

Dr. Bittker advised the committee that he did have a concern of a possible conflict of interest, of the energies which would have to be expended and of the sacrifice of fees and time involved.

Dr. Albert Eckstein, on behalf of BOMEX, spoke to the committee, advising that BOMEX felt a certain lack of ability and expertise in evaluating and investigating problems relating to impaired physicians and were desirous of obtaining the help and services of this committee.

Following a lengthy discussion by the membership,

IT WAS MOVED AND CARRIED, AS A CONSENSUS POSITION OF THE BOARD OF MEDICAL EXAMINERS AND THE PHYSICIAN REHABILITATION COMMITTEE, THAT APPROVAL BE REQUESTED FROM THE BOARD OF DIRECTORS OF ArMA AND FROM THE BOARD OF MEDICAL EXAMINERS AT THEIR RESPECTIVE MEETINGS IN DECEMBER OF 1978 THAT THE PHYSICIAN REHABILITATION COMMITTEE BE EMPOWERED AT ACT, NOT AS AN ARM OF, BUT, AS A BROKER FOR BOMEX TO RECOMMEND, WHEN REQUESTED IN SELECT CASES OF PHYSICIAN IMPAIRMENT, PHYSICIANS, INCLUDING MEMBERS OF SUCH COMMITTEE, TO ACT AS COMMISSIONERS OR CONSULTANTS; AND IN INSTANCES WHERE PHYSICIANS FROM THE PHYSICIAN REHABILITATION COMMITTEE ARE REQUESTED TO PERFORM SUCH FUNCTION THEY BE PERMITTED TO WITHDRAW FROM PARTICIPATING AS A COMMITTEE MEMBER DURING SUCH PERIOD OF PERFORMANCE.

It was further the consensus of opinion that the foregoing motion be submitted to legal counsel for BOMEX and the Association to determine what, if any, legal ramifications might result from assuming such a position; and that such opinions be submitted to both the Board of Directors of ArMA and the Board of Medical Examiners to be available for consideration in conjunction with the foregoing motion.

COMMITTEE MEMBER PRESENTATIONS

The Chairman reminded the committee that at the April meeting several assignments had been made to committee members to contact various medical organizations regarding the functions of the committee. With the exception of Stephen C. Scheiber, M.D. and Walter B. Tomlinson, M.D., who were not present at the meeting, reports regarding the contacts and reactions received were made by the following persons: Thomas E. Bittker, M.D., Bruce E. Robinson, Harrison G. Butler, M.D., Everett W. Czerny, M.D., B. Ross Landess, M.D., Laurence M. Linkner, M.D., and Louis E. Young, M.D.

Additionally, as a portion of his report to the committee, Dr. Young read into the record the following statement presented by him to St. Joseph's Hospital in Tucson at the time of such contact.

"THE PHYSICIAN'S REHABILITATION COMMITTEE

The Physician's Rehabilitation Committee has been in existence for a number of years. It is a committee made up of physicians who have volunteered their services to the Arizona State Medical Society to help their fellow physicians who are not in good health.

There are representatives on the committee from each county and eash specialty.

The committee is a separate committee and is not part of the Board of Medical Examiners. The committee's primary objective is to help the physician who has become ill, regardless of cause, to regain his health and return to a practice which is acceptable to his peers and his community.

Most of our physicians are well acquainted with their moral and ethical obligation to report physicians who are practicing and who are obviously not in good health to the degree that the treatment that they are giving is below the standard of good practice for our community. There are several members of the Physician's Rehabilitation Committee on the staff.

When it is obvious that the practicing physician's health is impaired or that there are changes in his practice or habits that are disturbing to our working personnel it is felt that these things should be reported immediately. It is only by prevention and early intervention that potential incidents can be avoided. It should be pointed out that under certain circumstances the physician himself may not be aware of early changes in his methods or caliber of administering what is considered to be good health care. When these refined changes become apparent to his peers or personnel working within the hospital it is felt that the individual nurse, employee, patient, or other concerned person, report these things. These things are simply reported to Administration, to the Chief of Staff, to one's supervisor, or directly to the County or State Medical Society.

The reporting individual need not disclose their identity or in certain circumstances may be very willing to openly disclose certain indidents that may be of a very serious nature. The committee is so designed that early intervention can and will occur and reports of this intervention are made back to the reporting individual. The anonymity of the source can be very discreetly withheld.

The distressed physician may not be himself aware of his disabilities. It is the committee's feeling that we are all morally obligated to protect our patient and to help our fellow physician and fellow employees when they are obviously in need.

The committee and its representatives stand ready to help you to help others. It is hoped that everyone will cooperate in this now national effort to help the impaired physician regain good health and to maintain our standard of practice and to protect our patients from potential hazard."

Dr. Young further reported that he had been

1979

INTERNATIONAL CATARACT SURGERY SYMPOSIUM

February 5, 6, 7

LaPosada Resort Hotel — Scottsdale, Arizona

sponsored by —

Arizona Foundation for Ophthalmic Research and Education

FACULTY

D. Peter Choyce *England*	M. U. Dardenne *Germany*	Marvin L. Kwitko *Canada*
Michael Blumenthal *Israel*	Richard P. Kratz *United States*	Donald L. Praeger *United States*
John H. Sheets *United States*	Robert M. Sinsky *United States*	Ronald W. Barnet *United States*

Each member of the faculty will describe his own methods of cataract surgery - with and without lens implants - and management of complications.

Mr. Choyce will give a special presentation about his work with Keratoprotheses.

LECTURES AND WORKSHOPS

- When is intracapsular extraction preferred to extracapsular.
- When are angle supported lenses preferred.
- What is the status of posterior chamber lenses.
- What is the role of A-scan biometry.
- What is the treatment for cystoid macular edema.
- Does the Choyce MK IX lens make the MK VIII obsolete.

This symposium is designed to coordinate with "Frontiers of Ophthalmology" February 8, 9, 10. Physicians may attend both meetings and receive 36 hours CME credit.

For further information, write:
Frances Gould, Symposium Coordinator
AFORE
421 North 18th Street, Suite 105
Phoenix, Arizona 85006
Phone: (602) 257-1077

requested to submit this statement for publication in the St. Joseph's Times and it was the consensus of opinion of the membership that the statement be offered for that publication as well as any others so requesting.

1979ArMA ANNUAL MEETING

Auxiliary Program

Dr. Clymer reported on the program planned to be presented by the Auxiliary during the annual meeting, "The Physician's Family Faces the '80's" and urged the committee members, if approached by the Auxiliary, to give serious consideration to participation in the program in an effort to make it a beneficial portion of the meeting.

Physical Fitness Program

The committee was advised that Dr. Bittker would be presenting a program during the annual meeting entitled "Taking Care of Ourselves; A Total Fitness Approach for Physicians and Their Spouses."

AMA's THIRD NATIONAL CONFERENCE ON " THE IMPAIRED PHYSICIAN"

A brief report was given regarding the AMA's Third National Conference on "The Impaired Physician," which had been attended by Drs. Bittker, Scheiber and Young. Dr. Young was asked to prepare his impressions of the conference in written form for submission to the committee.

OTHER BUSINESS

Request from Murray A. Katz, M.D.

Dr. Bittker advised the committee that Dr. Katz had expressed a desire to participate on the committee and Drs. Young and Clymer were requested to meet with Dr. Katz at their convenience to preliminarily discuss such participation and report back to the committee regarding such discussion.

60 Minutes

Dr. Bittker advised the committee that, although he had not been advised as yet regarding an airing date, he had recently been interviewed by "60 Minutes."

Paul B. Borgeson, M.D.

Dr. Borgeson, at the Chairman's request, briefly addressed the members regarding his first impressions as a new member of the committee.

Next Meeting

It was agreed that the next meeting of the committee would be held at 10:00 a.m. on Saturday, Febraury 3, 1979 at the Association offices.

EXECUTIVE COMMITTEE

The meeting of the Executive Committee of the Arizona Medical Association, Inc. held at 810 West Bethany Home Road, Phoenix, Arizona, on Friday, November 17, 1978, a quorum being present, convened at 6:40 p.m., Richard L. Dexter, M.D., President and Chairman, presiding.

DEPARTMENT OF HEALTH, EDUCATION & WELFARE'S HEALTH CARE FINANCING ADMINISTRATION PROGRAMS

Philip Nathanson, Regional Administrator of the Health Care Financing Administration of the Dept. of HEW, addressed the committee relative to the three basic objectives of this administration: 1) to improve Medicare and Medicaid programs, 2) to form a framework for national health insurance, and 3) to use Medicare/Medicaid reimbursement policies to constrain health care costs, briefly outlining the accomplishments made during the past 20 months regarding each objective, as well as touching on their many plans and hopes for future improvement.

Following Mr. Nathanson's presentation, Dr. D. P. McDonald spoke to the membership regarding his role as Chief Medical Officer for the Health Standards & Quality Bureau.

DEPARTMENT OF HEALTH SERVICES

Certificate of Need

Dr. Dandoy reported to the committee regarding the effort which is to be commenced within the next week regarding rewriting of the certificate of need statutes.

State Mental Hospital

This past week the state mental hospital was the site of a survey, in which Dr. D. P. McDonald has participated, being done to define problems and make recommendations regarding deficiencies. Dr. Dandoy felt the survey had been most beneficial and would hopefully result in large improvements.

Department of Corrections

Dr. Dandoy advised the committee that the Department of Corrections had recently employed a much-needed Medical Director, Dr. Ian Louden.

Crippled Children's Services

In what she felt was a most beneficial meeting, Dr. Dandoy met last week with the Pediatric Society regarding the Crippled Children's Services program and problems that Society wished to express or discuss.

Legionnaires' Disease

Dr. Dandoy recently attended a three-day national conference on Legionnaires' Disease in Atlanta, Georgia and was hopeful of being able to offer to the Scientific Assembly Committee some type of program on that subject to be included as a portion of the 1979 Annual Meeting.

Pesticide Poisonings

Dr. Dandoy made a brief statement regarding the recent testing done on several Scottsdale residents, informing the committee that the results of those tests were deemed "inconclusive."

AMERICAN MEDICAL ASSOCIATION INTERIM SESSION

Discussion was held regarding the Interim Session of the AMA scheduled for December 3-6, 1978, with Dr. Dexter briefly outlining the AMA's position on the chiropractic and other issues. Additionally, the delegates and alternates present at the meeting discussed briefly with the committee such matters as national health insurance and code of ethics.

GOVERNMENTAL SERVICES COMMITTEE

The committee received and reviewed the recommendation of the Governmental Services Committee regarding the calling of press conferences and, following discussion,

IT WAS MOVED AND CARRIED THAT THE RECOMMENDATION OF THE GOVERNMENTAL SERVICES COMMITTEE TO CALL PRESS CONFERENCES TO REFUTE FALSE ALLEGATIONS AGAINST THE MEDICAL PROFESSION AND TO PROMOTE THE PRACTICE OF MEDICINE TO THE PUBLIC BE REFERRED TO THE PUBLIC RELATIONS COMMITTEE FOR REVIEW AND ACTION.

COMMON CAUSE

Request of Common Cause dated November 8, 1978 re: rules changes in Arizona Legislature. RECEIVED.

Tenuate® Ⓒ IV
(diethylpropion hydrochloride NF)

Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of mono amine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect, rather, the drug should be discontinued Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe There are reports of patients who have increased the dosage to many times that recommended Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression, changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy*: Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children*: Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary

ADVERSE REACTIONS: *Cardiovascular*: Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System*. Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic*: Urticaria, rash, ecchymosis, erythema. *Endocrine* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System*. Bone marrow depression, agranulocytosis, leukopenia *Miscellaneous*: A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily, swallowed whole, in midmorning Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

Direct Medical Inquiries to
MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215, U.S.A.

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References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215 2. Hoekenga, M.T., O'Dillon, R H., and Leyland, H.M A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs. Florence, Italy. Jan. 20-21. 1977.

Merrell

8-3921 (Y587A)

Whether overweight is a complicating factor… or just uncomplicated overweight.

Tenuate® Dospan® Ⓒ IV
(diethylpropion hydrochloride NF)
75 mg. controlled-release tablets

A useful short-term adjunct in an indicated weight loss program.

Overweight patients in certain diagnostic categories often require strict obesity control. Diethylpropion hydrochloride has been reported useful in obese patients with hypertension, symptomatic cardiovascular disease, or diabetes. While it is not suggested that Tenuate in any way reduces these complications in the overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. (Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.)

In uncomplicated obesity.

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

Clinical effectiveness.

The anorexic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.[1] And the unique chemistry of Tenuate provides "…anorexic potency with minimal overt central nervous system or cardiovascular stimulation."[2] Compared with the amphetamines, diethylpropion has minimal potential for abuse.

Tenuate—it makes sense. And it's responsible medicine.

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For prescribing information see opposite page

EMPIRIN® COMPOUND
$\bar{c}$ CODEINE

Each tablet contains: aspirin, 227 mg; phenacetin, 162 mg; and caffeine, 32 mg; plus codeine phosphate in one of the following strengths: #4—60 mg (gr 1); #3—30 mg (gr ½); #2—15 mg (gr ¼); and #1—7.5 mg (gr ⅛). (Warning—may be habit-forming).

CIII

Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

PROFESSIONAL COMMITTEE

Dr. Dexter addressed the committee rearding the program of the Pima Council To mmunize Arizona's Children and the motion eceived from the Professional Committee reommending to the Board of Directors enorsement of financial support for the coninuation of such program.

IT WAS MOVED AND CARRIED TO CCEPT THE MOTION OF THE PROESSIONAL COMMITTEE TO RECOMIEND TO THE BOARD OF DIRECTORS NDORSEMENT OF FINANCIAL SUPPORT OR THE CONTINUATION OF THE PIMA OUNCIL TO IMMUNIZE ARIZONA'S HILDREN PROGRAM AND REFER THE AME TO THE FINANCE COMMITTEE OR ITS CONSIDERATION AND ACTION.

At this point, Dr. Dandoy offered to obtain nd furnish to the Finance Committee for its onsideration the future funding which the ima Council anticipates it will receive from tate and federal levels.

WESTERN PHYSICIANS PURCHASING ASSOCIATION

urchasing Committee

Bruce Robinson reported to the committee hat Melvin Roberts, M.D., had found it ecessary to decline his invitation to particiate on the Purchasing Committee for WPPA; owever, Dr. Roberts had recommended Lawence M. Haas, M.D. to serve on such ommittee.

IT WAS MOVED AND CARRIED THAT LAWRENCE M. HAAS, M.D., BE EXTENDED AN INVITATION TO SERVE ON THE PURCHASING COMMITTEE FOR THE WESTERN PHYSICIANS PURCHASING ASSOCIATION.

OTHER BUSINESS

Governmental Services Committee

Dr. Dexter advised the committee regarding a recent address given by Dr. DePaoli to the Governmental Services Committee relative to legislative action and the necessity of constant awareness of all aspects of all legislative matters, and presented to the committee a recommendation from Governmental Services Committee that a full-time employee be hired, if financially feasible, to research legislation, health planning, and other government activities relative to medicine.

IT WAS MOVED AND CARRIED TO ACCEPT THE CONCEPT OF HIRING A FULL-TIME EMPLOYEE, IF FINANCIALLY FEASIBLE, TO RESEARCH LEGISLATION, HEALTH PLANNING, AND OTHER GOVERNMENT ACTIVITIES RELATIVE TO MEDICINE AND THAT THE SAME BE SUBMITTED TO THE FINANCE COMMITTEE FOR FURTHER CONSIDERATION AND ACTION.

The committee went into executive session at this point.

HOUSESTAFF REQUEST

IT WAS MOVED AND CARRIED TO AUTHORIZE THE HOUSESTAFF SECTION TO UTILIZE UP TO $300.000 OF THEIR PRESENT BUDGET FOR THE PURPOSE OF FUNDING A SECOND RESIDENT AT THE DECEMBER MEETING OF THE AMERICAN MEDICAL ASSOCIATION.

Future Medical Meetings

CONTINUING MEDICAL EDUCATION

The following institutions and organizations have been accredited for their continuing medical education programs by the Liaison Committee on Continuing Medical Education.

- Arizona Heart Institute
- Arizona Medical Association, Inc.
- Arizona State Hospital, Phoenix
- Desert Samaritan Hospital, Mesa
- Good Samaritan Hospital, Phoenix
- Health Maintenance Associates
- Phoenix Indian Medical Center
- Phoenix Psychiatric Council
- Maricopa County General Hospital, Phoenix
- Memorial Hospital, Phoenix
- St. Luke's Hospital & Medical Center, Phoenix
- St. Joseph's Hospital & Medical Center, Phoenix
- Tucson Hospitals Medical Education Program, Tucson
- U of A College of Medicine
- Veterans Administration Center, Prescott
- Veterans Administration Hospital, Phoenix

The accredited institutions and organizations above produce a variety of continuing medical education programs. Each accredited institution and organization is responsible for designating which of these programs meet ArMA's requirements for Category 1 credit. Physicians who participate in programs which are designated Category 1 by accredited institutions will receive Category 1 credit toward the ArMA Certificate in CME and the AMA's Physician's Recognition Award.

JANUARY

Recent Advances in Geriatric Psychiatry
January 20, 1979, Maricopa County General Hospital, Phoenix, AZ. Sponsor: Maricopa County General Hospital. Contact: Medical Education Office, Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 4 hours of categor 1 credit.

Bone Imaging: A Clinical Practicum
January 21,1979, Phoenix, AZ. Sponsor: The Society of Nuclear Medicine. Contact: Karen J. Chang, Society of Nuclear Medicine, 475 Park Ave., South, New York,, NY 10016. Approved for 5 hours of category 1 credit.

Critical Care of Neurological and Neurosurgical Emergencies
January 25-27, 1979. Camelback Inn, Phoenix, AZ. Sponsor: St Joseph's Hospital and Medical Center, Barrow Neurological Institute. Contact: Richard A. Thompson, M.D., Chairman, 350 W. Thomas Rd., Phoenix, AZ 85013. Approved for category 1 credit.

5th Annual MCGH Urological Seminar
January 27 & 28, 1979. Doubletree Inn, Scottsdale, AZ 85251. Sponsor: Maricopa County General Hospital. Contact: Medical Education Office, Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 18 hours of category 1 credit.

Selected Horizons in Infection Diagnosis and Laboratory Management
January 27-28, 1979, Tucson Marriott Hotel, Tucson, AZ Sponsors: Arizona Society of Pathologists and the American Society of Clinical Pathologists. Contact: Carol Turner, 810 W. Bethany Home Rd., Phoenix, AZ 85013. (602) 246-8901. Approved for 7 hours of category 1 credit.

Medical History Society of Arizona
January 29, 1979, 7:30 p.m. Contact: William C. Weese, M.D. President, (602) 265-000.

FEBRUARY

Southwest Desert Symposium In Anesthesiology
February 2-4, 1979. Doubletree Inn, Tucson, AZ. Sponsor: U of A College of Medicine, Dept. of Anesthesiology, and Office of Continuing Medical Education. Contact: Office of Continuing Medical Education. U of A College of Medicine, Health Sciences Center, Tucson, AZ 85724. Approved for 17 hours of category 1 credit.

Selected Topics In Neuroradiology
February 7-9, 1979. San Diego, CA. Sponsor: San Diego Radiology Research & Education Foundation and the American College of Radiology. Contact: Mary J. Ryals, Radiology, P.O. Box 2305, La Jolla, CA 92038. (714) 453-7500, Ex. 3711. Approved for 22½ hours of category 1 credit.

Fifth Annual Frontiers in Ophthalmology Seminar
February 8,9,10, 1979. Mountain Shadows Resort. Sponsor: St. Luke's Hospital Medical Center. Contact: Christine Campbell, Seminar Coordinator, St. Luke's Hospital Medical Center, 525 N. 18th St., Phoenix, AZ 85006 (602) 258-7373. Ext. 311. Approved for 18 hours of category 1 credit.

4th Annual Seminar Radiology of the Abdomen
February 9,10,11, 1979. Safari Hotel, Scottsdale, AZ. Sponsor: Maricopa County General Hospital. Contact: Austin R. Sandrock, M.D., Program Chairman, Dept. of Radiology, Maricopa County General Hospital, 2601 E. Roosevelt St., Phoenix, AZ 85008. Approved for 15 hours of category 1 credit.

Second Annual Postgraduate Course in OB/GYN
February 14-16, 1979, Scottsdale Hilton Hotel, Scottsdale, AZ. Sponsors: Phoenix OB/GYN Society and Dept. of OB/GYN Maricopa County General Hospital. Contact: Secretary, Phoenix OB/GYN Society, 333 E. Virginia, Ste. 222, Phoenix, AZ 85004, (602) 257-9218. Approved for category 1 credit.

Advanced Cardiac Life Support Programs Provider Course
February 16 & 17, 1979. Arizona Medical Association, Inc., 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor. Arizona Affiliate of the American Heart Association. Contact: Carol Turner at the Arizona Medical Association. Approved for 16 hours of category 1 credit.

Health Policy and Chronic Illness: The National Debate
February 17 & 18, 1979. Sherton-Place Hotel, San Francisco, CA. Sponsor: University of California, San Francisco Schools of Medicine. Contact: Ms. Bruce, University of California, San Francisco Continuing Education in Health Sciences, 1343 3rd Ave., San Francisco, CA 94143.

International Cardiovascular Congress Non-Invasive Diagnosis
February 19,20,21, 1979. Scottsdale Center for the Arts, Scottsdale, AZ. Sponsor: Arizona Heart Institute. Contact: Arizona Heart Institute, P.O. Box 10,000. Phoenix, AZ 85064 Approved for 17 hours of category 1 credit.

Medical Progress: A review of Advances in Medicine in Past 5 Years
February 22-24, 1979, Casa Blanca Inn, Scottsdale, AZ. Sponsor: Maricopa County General Hospital. Contact: Medical Education Office, Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for I5 hours of category 1 credit.

Current Advances in Obstetrics and Gynecology
February 14-16, 1979. Scottsdale Hilton Hotel, Scottsdale, AZ. Sponsor: Maricopa County General Hospital. Contact: Medical Education Office, Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 18 hours of category 1 credit.

Advances in Internal Medicine
February 22-24, 1979, Casa Blanca Inn, Scottsdale, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

1979 Annual Scientific Meeting: Arizona Society of Anesthesiologists
February 24,25,1979. Radisson Scottsdale Resort, 7601 E. Indian Bend Rd., Scottsdale, AZ. Sponsor: College of Medicine, Tucson, AZ & Arizona Society of Anesthesiologists. Approved for 10 hours of category 1 credit.

Pediatric Update 1979
February 26 - March 1, 1979. Scottsdale Sherton Inn, Scottsdale, AZ. Sponsor: St. Joseph's Hospital & Medical Center, Phoenix, AZ. Contact: Tracy L. Trotter, M.D., Dept. of Pediatric Education, St. Joseph Hospital & Medical Center, 350 West Thomas Rd., Phoenix, AZ 85013. Approved for 16 hours of category 1 credit.

MARCH

Day of G.I. & Liver Disease
March 2, 1979. Camelback Inn, Scottsdale, AZ. Sponsor: St Joseph's Hospital and Medical Center. Contact: Ethelann Murray, M.D., St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Approved for 6 hours of category 1 credit.

New Mexico Metabolism Symposium
March 8, 9, & 10, 1979, Taos, New Mexico. Contact: Office of Education, Lovelace Medical Center, Albuquerque, New Mexico. (505) 842-7353.

Purgatory Colorado Medical Ski Symposium
March 8 — 11, 1979. Ramada Inn, Durango, Co. Sponsor: Albuquerque Academy of Family Physicians. Contact: Albuquerque Academy of Family Physicians, 2650 Yale, S.E., No. 10, Albuquerque, N.M. 87105. Approved for 12 hours of category 1 credit.

Psychopharmacology in Children
March 9—11, 1979, Double Tree Inn, Tucson, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

Clinical Recognition and Management of Heart Disease — 1979
March 22,23 & 24, 1979. U of A Health Sciences Center, Main Auditorium. Sponsor: U of A College of Medicine. Contact: Registrar, American College of Physicians, 420 Pine St., Philadelphia, PA 19104.

Third Annual Southwestern Cardiovascular Symposium — 1979
March 28, 29, & 30, 1979. The Reistry Resort, Scottsdale, AZ. Sponsor: St. Luke Hospital Medical Center, 525 N. 18th St. Phoenix, AZ 85006. Contact: Public Relations, St. Luke's Hospital. Approved for 14 hours of category 1 credit.

Second International Conference on the Adjuvant Therapy of Cancer
March 28—31, 1979. Tucson Convention Center, Tucson, AZ. Sponsor: U of A College of Medicine, Cancer Center Division. Contact: Cancer Center Division, U of A College of Medicine, Tucson, AZ 85724. Approved for 23 hours of category 1 credit.

Second Annual Symposium on Aging
March 31 and April 1, 1979. Sheraton-Place Hotel, San Francisco, CA Sponsor: Univ. Of California, San Francisco Schools of Medicine. Contact: Ms. Bruce, Univ. of California, San Francisco Continuing Education in Health Sciences, 1343 3rd Ave, San Francisco, CA 94143. Approved for category 1 credit.

APRIL

Fifteenth Annual Arizona Chest Symposium
April 6,7,8, 1979. Doubletree Inn, Tucson, AZ. Sponsor: College of Medicine, U of A and Tucson Medical Center. Contact: Linda Alpert, R.N., Symposium Coordinator Tucson, Medical Center, P.O. Box 6067, Tucson, AZ 85733. Approved for category 1 credit.

88th Annual Meeting: Arizona Medical Association
April 25—29, 1979. Sponsor: Arizona Medical Association, Inc. Contact: Bruce E. Robinson, Executive Director, 810 W. Bethany Home Rd., Phoenix, AZ 85014. Approved for category 1 credit.

MAY

Fourth Annual Update Primary Care
May 2-5, 1979, Arizona Health Sciences Center, Tucson, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

MONTHLY OR WEEKLY

Shrine Medics Meeting
Second Tuesday of each month, Doctors Hospital, 5:45 p.m. J. South Classroom Sponsor: Shrine Medics. Contact: Robert C Briggs, M.D., 5121 N. Central Ave., Phoenix AZ 85012.

Office Psychiatry for the Primary Provider
2nd Monday of month, 4811 N. 7th Street Phoenix, AZ. Sponsor: Arizona Health Plan Contact: T.R. Bittker, M.D., Box 5000, Phoenix, AZ 85010. Approved for category credit.

Counter Transference Group
Weekly, Thurs. 8—10 p.m. Sponsor: Phoenix Psychiatric Council. Contact: James E Campbell, M.D., 5051 N. 34th St., Phoenix, AZ 85018. Approved for 2 hours category credit.

Monthly Meeting of Tucson Radiologists
Last Tues. of month. Plaza International Tucson, AZ. Sponsor: U of A Medical Center Dept. of Radiology. Contact: Irwin M Freundlich, M.D., U of A Health Sciences Center, Dept. of, Radiology, Tucson, AZ 85724. Approved for 2 hours category 1 credit.

Pediatric Grand Rounds
Tuesday 7:30-8:30 a.m in Phoenix: 1s Tues.—Phoenix Indian Hospital, 2nd Tues.—Maricopa County Hospital, 3rd Tues.—Good Samaritan Hospital, 4th Tues.—St. Joseph's Hospital. Sponsor: Maricopa County Hospital (Phoenix Hospital's Affiliated Pediatric Program). Contact: J. Kipp Charlton, M.D., 2601 E. Roosevelt, Phoenix AZ 85008. Approved for 1 hour per session category 1 credit.

Review of Forensic Pathology Current Case, Special Topics
Thursday, weekly, 11 a.m., 120 S. 6th Ave. Phoenix, AZ. Sponsor: Arizona Society of Pathologists. Contact: H.H. Karnitschnig M.D., 120 S. 6th Ave., Phoenix, AZ. Approved for 1 hour per session category 1 credit.

Staff Education Conference
Wednesdays, weekly, 1 p.m., Arizona State Hospital, Phoenix, AZ. Sponsor: Arizona State Hospital. Contact: Howard E. Wulsin M.D., Arizona State Hospital, 2500 E. Van Buren, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

BARROW NEUROLOGICAL INSTITUTE

Medical Education
Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Sponsor: St Joseph's Hospital & Medical Center. Contact: John R Green, M.D. Approved for 1 hour category 1 credit.

Neurology Teaching Conference
Tuesdays, 8:30-9:30 a.m., Eighth Floor Conf. Room.

Neurosurgery Morbidity Conference
Wednesdays, 8:15-9:15 a.m., on first and third weeks, Eighth Floor Conference Room.

Neuro-ophthalmology Conference
Tuesdays, 7:30 a.m. in 8th floor neurology conference room.

Spinal Injury Conference
Wednesdays, 8:15-9:15 a.m., on second and fourth weeks, in Neuropathology Conf. Rm.—a multidisciplinary review of admission by neurosurgeons, orthopedists, and rehabilitation specialists

Neuropathology of Gross Specimens Conference
Thursday, 7:30-8:30 a.m. in the Morgue.

Neurology-Neurosurgical Clinical-Neuroradiological and Neuropathological Conference
Fridays, 8-9 a.m., First Floor Conference Rm.

Neuropathology or Neuroradiology Conferences
Friday, 9 a.m., Neuropathology in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

Neurorehabilitation Conference
Tuesdays, noon, 8th Floor Conference Rm.

Neurosurgical Journal Club
Saturdays, 9-11 a.m. in Eighth Floor Conference Rm.

CAMELBACK HOSPITAL

5055 N. 34th St., Phoenix, AZ 85018. Sponsor: Camelback Hospital. Contact: Medical Director.

Patient Staffing Conference
Three times weekly

DESERT SAMARITAN HOSPITAL

Wednesday evenings, 7 p.m. Sponsor: Desert Samaritan Hospital. Contact: L. A. Rosati, M.D., Laboratory, Desert Samaritan Hospital, Mesa, AZ 85202. Approved for category 1 credit.

GOOD SAMARITAN HOSPITAL

Clinical Cancer Conference
3rd Wednesday, every month, Butler Bldg. Conference Rm. Good Samaritan Hospital. Contact: John A. Bruner, M.D., 926 E. McDowell Rd., Phoenix, AZ 85006. Approved or 1 hour per session category 1 credit.

Pulmonary Disease Grand Rounds
Mondays, 12 Noon, D-5 North Conf. Rm., Good Samaritan Hospital, Phoenix, AZ. Sponsor: Pulmonary Disease Teaching Service, Good Samaritan Hospital. Contact: Bernard E. Levine, M.D., Pulmonary Function Laboratory, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour category 1 credit.

MARICOPA COUNTY GENERAL HOSPITAL

2601 E. Roosevelt, Phoenix, AZ 85008. Sponsor: Maricopa County General Hospital. Contact: H. F. Lenhardt, M.D., Dir. of Medical Education. Approved for category 1 credit.

Recent Advances in Geriatric Psychiatry
January 20, 1979. Maricopa County General Hospital

5th Annual MCGH Urological Seminar
January 27 & 28, 1979. Doubletree Inn, Scottsdale, AZ 85251.

Current Advances in Obstetrics and Gynecology
February 14, 15 & 16, 1979, Scottsdale Hilton Hotel, Scottsdale, AZ.

Medical Progress: A Review of Advances in Medicine in the Past 5 Years
Feb. 22, 23 &, 24, 1979. Carefree Inn, Carefree, AZ 85331.

The Head
Presented by Dept. of Radiology, Feb. 9, 10 11, 1979. Doubletree Inn, Scottsdale, AZ 85251

MEMORIAL HOSPITAL

1201 S. 7th Ave., Phoenix, AZ 85036. Sponsor: Memorial Hospital. Approved for category 1 credit.

Month Medical Education Seminar
Third Monday, 6:30 p.m., Kiva Conference Rm. Contact: George Scharf, M.D.

Tumor Board Conference
Every Friday at Noon, Kiva Conference Rm. Contact: Howard Kimball, M.D.

SCOTTSDALE MEMORIAL HOSPITAL

7300 E. 4th St., Scottsdale, AZ 85251. Sponsor: Scottsdale Memorial Hospital. Contact: W. S. Wlliams, M.D., Director of Medical Education

Clinical Pathological Conference
4th Monday, monthly, 12:45 p.m.

Family Practice Conference
1st Monday, monthly, 12:45 p.m.

Medical Grand Rounds
3rd Monday, monthly, 12:45 p.m.

Morbidity & Mortality Conference
2nd Monday, monthly, 12:45 p.m.

ST MARY'S HOSPITAL & HEALTH CENTER

1601 W. St. Mary's Rd., Tucson, AZ 85703. Sponsor: St. Mary's Hospital & Health Center. Contact: see below.

Cardiology Conference
Every Friday 8-9 a.m., Century Rm. A. Contact: Anthony L. Forte, M.D.

Monthly Specialty Conference of the Department of Surgery
First Monday, monthly, 7:30 a.m. Century Rm. A. Contact: Medical Staff Office. Approved for 1 hour of category 1 credit

Grand Rounds: Medical Surgical, Family Practice, Pathology, Radiology
Weekly, Thursday, 7-8:30 a.m. Contact: Richard A. Silver, M.D. Approved for 1 hours of category 1 credit.

U OF A HEALTH SCIENCES CENTER

Sponsor: U of A College of Medicine, Tucson, AZ 85724. Contact: See below. Approved for category 1 credit.

Clinical Immunology, Allergy & Rheumatology Rounds
Every Friday, Noon-1 p.m. Contact: John Boyer, M.D., Dept. of Internal Medicine.

Cerebrovascular Disease Conference
Mondays, 5-6 p.m., weekly, Rm. 5505. Contact: Wesly Moore, M.D.,Depts. of Surgery, Nurology & Radiology.

Dean's Clinical Rounds
October 18, 1978, Main Auditorium, UAHSC. Contact: Louis J. Kettel, M.D.

Endocrinology Seminar
Every Thursday, Noon-1 p.m., 1st, 3rd & 5th Thursday, Room N318, VA Hospital. 2nd & 4th Thursday, Room 6505, Tucson Medical Center. Contact: Dept. of Internal Medicine.

Hematology-Oncology Clinical Conference
Every Tuesday, Noon-1 p.m., 1st, 3rd & 5th Tuesdays, Rm 6505, Tucson Medical Center. 2nd & 4th Tuesdays, Rm. N318, VA Hospital. Contact: Sidney Salmon, M.D., Dept. of Internal Medicine.

Joint Thyroid Clinic Conference
1st & 3rd Wednesdays of every month. AHSC, Rm. 6505. Contact: Sidney Werner, M.D., Dept. of Internal Medicine, Endocrinology Section.

Medical Grand Rounds
Every Wed., Noon-1 p.m., 1st, 3rd, & 5th Wed., Staff Conf. Room, VA Hospital. 2nd & 4th Wed.,Rm. 5403, UAHSC. Contact: Jay Smith, M.D., Dept. of Internal Medicine.

Nuclear Medicine
Thursday, 7:30 a.m., Radiology Conf. Rm., UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Diagnostic Radiology.

Neurology Grand Rounds
/Every Friday, Noon, 1st, 3rd, & 5th Fridays, UAHSC, Rm. 7505. 2nd & 4th Fridays, VA Hospital. Contact: William A. Sibley, M.D., Dept. of Neurology.

Neuropathology Review Conference
Thursdays, 8:30 a.m., Rm. 5120, UAHSC. Contact: Peter C. Johnson, M.D.

Neurosciences Seminar
Every Friday, 7:30 a.m.,UAHSC, Rm 7505. Contact: Colin R. Bamford, M.D., or Jose F Laguna, M.D., Dept. of Neurology.

Pathology Seminar
Friday, 4:30-5:30 p.m., Rm. 5120, UAHSC. Contact: Paul Finley, M.D., Dept. of Pathology.

Tucson Pathologist Conference
First Monday of the Month, 7:30-9 p.m. Rotation between Tucson Pathology Conf. Rms. Contact: Anna Graham, M.D., Tucson Pathologists.

Pediatric Grand Rounds
Every Tuesday, 12:30-1:30 p.m. Alternates between Tucson Medical Center & UAHSC. Contact: Hugh Thompson, M.D., Dept. of Pediatrics.

Problem Case Workshop
3rd Monday of each month, 7:30 a.m., Rm 4410, UAHSC. Contact: H. E. Cross, M.D., Ph.D., Div. Of Ophthalmology.

Psychiatric Grand Rounds
Every Wednesday, Sept. to May 4, 5:30 p.m., Rm8403 UAHSC. Contact: Alan Levenson, M.D., Dept. of Psychiatry.

Chest Radiology
Monday, 5-6 p.m., weekly, Rm 1535F, UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Gastrointestinal Radiology
Mondays, 7:30 a.m., weekly except for summer months. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Radiation Oncology Planning Conference
Friday, weekly, 8:30-10 a.m., UAHSC, Rm. 0655. Contact: Robert S. Heusinkveld, M.D., Radiation Oncology Section.

Radiology-Rheumatology Conference
Thursday, 8 a.m., UAHSC, Library Rm.1535C. Contact: Irwin M. Freundlich, M.D. Dept. of Radiology.

Vascular Radiology
Radiology Interesting Case Conference
Thursday, Noon, VA Hospital. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Resident's Conference
Wednesday, weekly 5-6 p.m., Diag. Radiology Conf. Rm. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology

Trauma Conference
Every Thursday,4-5 p.m. UAHSC, Rm. 5505. Contact: Martin Silverstein, M.D., Dept. of Surgery.

Grand Ward Rounds—Trauma
Every Tuesday, 8 a.m., UAHSC. Contact: Martin Silverstein, Surgery Dept., Trauma Section.

Monthly Meeting Tucson
Ultrasonography Group
First Wed. of month, 4:30-5:30 p.m., UAHSC. Contact: Irwin M. Freundlich, M.D.

Tucson Urological Society
Scientific Meeting
Monthly. Contact: George W. Drach, M.D., Depts. of Surgery & Urology.

General Urology Conference
Tuesday 5-6 p.m. Thursday, Noon-1:30 p.m. UAHSC Meeting Rooms & VA Hospital. Contact: George W. Drach, M.D., Dept of Surgery/Urology Section.

VETERANS ADMINISTRATION HOSPITAL

7th St. and Indian School Rd., Phoenix, AZ 85012. Sponsor: VA Hospital. Contact: Jasper L. McPhail, M.D. Approved for Category 1 credit.

Academic Surgery Conference
Each Thursday — 2 p.m. — C435, Dr. Cannon, Ext. 493.

Cardiology Conference
2nd Thursday — 1 p.m. — T5, Dr. Habibzadeh, Ext. 348.

Cancer Symposium
Each Wednesday — 1 p.m. — T5, Dr. Berkley, Ext. 419.

Clinical Conference
4th Thursday of 3rd Month, (Mar. Jun., Sept., & Dec.), 1 p.m. — T5, Dr. Likos, Ext. 623.

Dermatology Conference
1st, 2nd, & 3rd Wednesday (usually, but is subject to change) 10 a.m. — C118, Dr. Roberts, Ext. 426.

G.I. Radiology Clinical
Correlation Conference 1st & 3rd Monday — 1 p.m. — C435, Dr. Sanowski, Ext. 618.

G.I. Grand Rounds
Ech Tuesday — 1 p.m. — T5, (4th Thursday with U of A Consultants) Dr. Sanowski, Ext. 618.

Medical Service Grand Rounds
Each Friday — 11 a.m. — T5, Dr. Zeller, Ext 272

Medical-Surgical Chest Conference
1st and 3rd Thursday — 1 p.m. — T5, Dr. Chowdhury, Ext. 388.

Medical-Surgical G.I. Conference
lst & 3rd Friday — 2 p.m. — 2123, Dr. Sanowski, Ext. 618.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery-Pathology Conference
Each Thursday — 2 p.m. — 2128, Dr. Cannon, Ext 493, & Dr. Likos, Ext. 623.

Urology-Pathology Conference
Each Wednesday — 7 a.m. — 2128, Dr. Likos, Ext. 623 & Dr. Pentenney, Ext., 417.

INTERNATIONAL CARDIOVASCULAR CONGRESS II

NON-INVASIVE DIAGNOSIS

PRESENTED BY THE ARIZONA HEART INSTITUTE

FEBRUARY 19, 20, 21, 1979
SCOTTSDALE CENTER FOR THE ARTS
SCOTTSDALE, ARIZONA, USA

PURPOSE:

Non-invasive techniques for the diagnosis of heart, arterial and venous diseases have become one of the fastest growing areas of medical science. Congress II brings together a distinguished international faculty and leading experts in a program of 88 scientific papers covering current techniques, instrumentation and results from leading centers in the United States, Canada, Europe, South America and Japan. All presentations will be in English.

TOPICS TO BE COVERED

I. Cerebrovascular Disease
II. Peripheral Vascular Arterial Disease
III. Peripheral Vascular Venous Disease
IV. Coronary Heart Disease
V. Valvular Heart Disease
VI. Congenital Heart Disease

Scientific sessions will include discussions on the use of Doppler, Stress Testing, Oculoplethysmography, Carotid Phonoangiography, Impedance Plethysmography, Vectorcardiography, Real Time Imaging, Echocardiography, Ultrasound Scanning, and other non-invasive diagnostic techniques.

FACULTY:

Included in the faculty will be such distinguished physicians as:

Loring Brock, M.D.
Denver, CO

H. H. G. Eastcott, M.D.
London, England

J. Gundersen, M.D.
Kristianstad, Sweden

Walter L. Henry, M.D.
Bethesda, MD

J. Keutel, M.D.
Bonn, West Germany

P. J. Kuijpers, M.D.
Nijmegen, The Netherlands

P. Rentrop, M.D.
Göttingen, West Germany

Jos Roelandt, M.D.
Rotterdam, The Netherlands

D. Eugene Strandness, Jr., M.D.
Seattle, WA

Louis Evan Teichholz, M.D.
New York, NY

H. Brownell Wheeler, M.D.
Worcester, MA

James S. T. Yao, M.D.
Chicago, IL

Program supported in part by Educational Grants from the Arizona Heart Institute Foundation and Marion Laboratories, Inc.

REGISTRATION:

Registration is open to physicians in all fields of medicine interested in non-invasive cardiovascular diagnosis. Internists, cardiologists, cardiac and vascular surgeons, family physicians, and other specialty groups will benefit from this international symposium on the state of the art.

FEES

Physicians: $200 *If fee paid in full by Jan. 1, 1979 - $150*
Residents, Interns, and Technicians: $100 *If fee paid in full by Jan. 1, 1979 - $75*
Registration fee includes lunches.

ACCREDITATION:

AMA
As an organization accredited for continuing medical education, the Arizona Heart Institute certifies that this continuing medical education activity meets the criteria for 17 credit hours in Category I of the Physician's Recognition Award of the American Medical Association.

AAFP
This Program is acceptable for 17 Elective hours by the American Academy of Family Physicians.

For registration information or information on hotel accommodations, write to:
ARIZONA HEART INSTITUTE/ INTERNATIONAL CARDIOVASCULAR CONGRESS II
P.O. Box 10,000 Phoenix, Arizona 85064

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- Gastroenterology (4 hrs.)
- New Drug Therapy & Trauma (4 hrs.)

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Advance registration required. Registration fee of $100.00 includes continental breakfast for two each morning and two hosted receptions. Registration deadline January 31, 1979. Limited to 100 participants.

For further information contact:
Albuquerque & Bernalillo County Medical Association
2650 Yale Blvd., SE Suite 103
Albuquerque, New Mexico 87106
Phone (505) 247-3711

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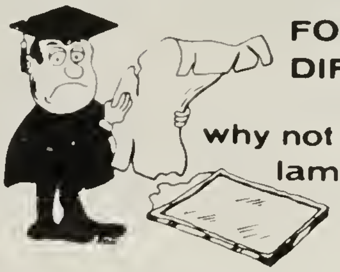

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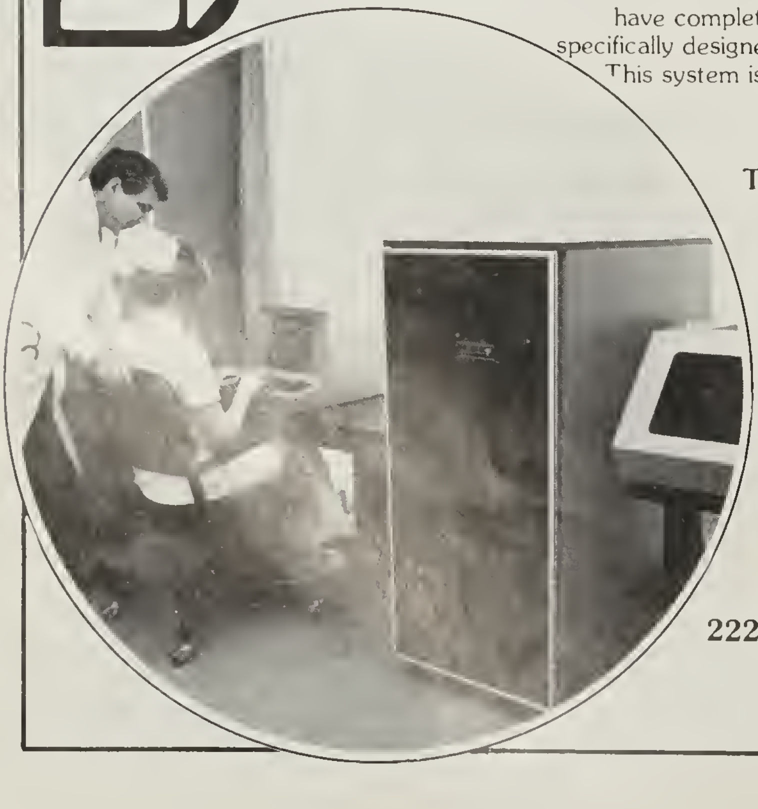

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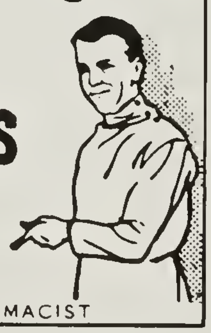

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Usage in Pregnancy: **Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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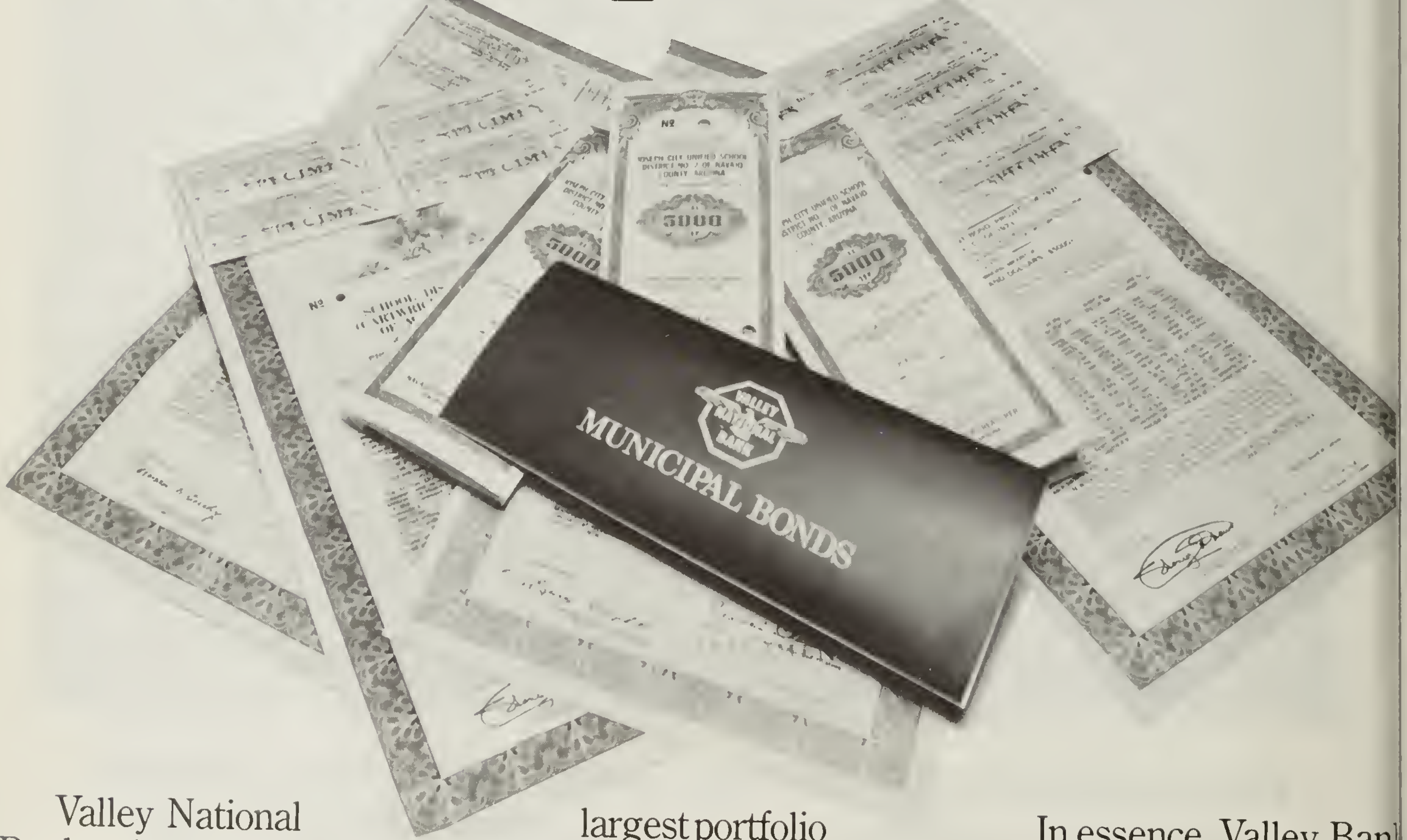

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NEW DIRECTIONS

Wednesday April 25

Board of Directors Meeting — 8 a.m.
House of Delegates Meeting 1st General Session — 10 a.m.
Reference Committee Meetings — 2 p.m.

Thursday April 26

"Physicians Families" - Special Program 2 p.m.
Annual Golf Tournament — 12 noon
Annual Tennis Tournament — I p.m.
5th Annual National Calliope Concert — 6 p.m.
Reception and Steak Fry — 7 p.m.

FRIDAY APRIL 27

House of Delegates 2nd General Session — 8 a.m.
Scientific Program begins — 2 p.m.
ArMPAC Reception and Banquet — 7 p.m.

Saturday April 28

Breakfast Panel — 7 a.m.
Scientific Program Resumes — 9 a.m.
President's Reception and Banquet — 7 p.m.

Sunday April 29

Breakfast Panel — 7 a.m.
Scientific Program Resumes — 9 a.m.
Meeting concludes — 12 noon

Tenuate® Ⓒ
(diethylpropion hydrochloride NF)

Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence.* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy*: Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children*: Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular*: Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System*: Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal*: Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic*: Urticaria, rash, ecchymosis, erythema. *Endocrine*: Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System*: Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous*: A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

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References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215 2. Hoekenga, M.T., O'Dillon, R.H., and Leyland, H.M.. A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy, Jan. 20-21, 1977.

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75 mg. controlled-release tablets

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*The safety and effectiveness of Motrin have not been established in patients with Functional Class IV rheumatoid arthritis (incapacitated, largely or wholly bedridden, or confined to wheelchair; little or no self-care).

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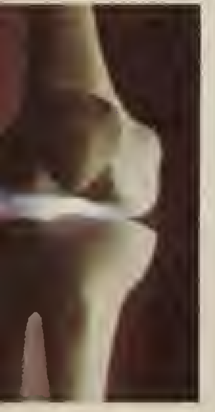


Motrin 400 TABLETS mg
ibuprofen, Upjohn

The confidence that comes from experience—
one more reason to prescribe Motrin.

Please turn page for a brief summary of prescribing information.

Upjohn The Upjohn Company, Kalamazoo, Michigan 49001

The confidence that comes from experience—
one more reason to prescribe

Motrin 400 mg TABLETS
ibuprofen, Upjohn

Indications and Usage: Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Contraindications: Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

Warnings: Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.
Drug interactions. *Aspirin* used concomitantly may decrease Motrin blood levels. *Coumarin:* Bleeding has been reported in patients taking Motrin and coumarin.
Pregnancy and nursing mothers: Motrin should not be taken during pregnancy or by nursing mothers.

Adverse Reactions

Incidence greater than 1%

Gastrointestinal: The most frequent type of adverse reaction occurring with Motrin (ibuprofen) is gastrointestinal (4% to 16%). This includes nausea*, epigastric pain*, heartburn*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness*, headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

Incidence: Unmarked 1% to 3%; *3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

Overdosage: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

Dosage and Administration: Suggested dosage is 300 or 400 mg t.i.d. or q.i.d. Do not exceed 2400 mg per day.

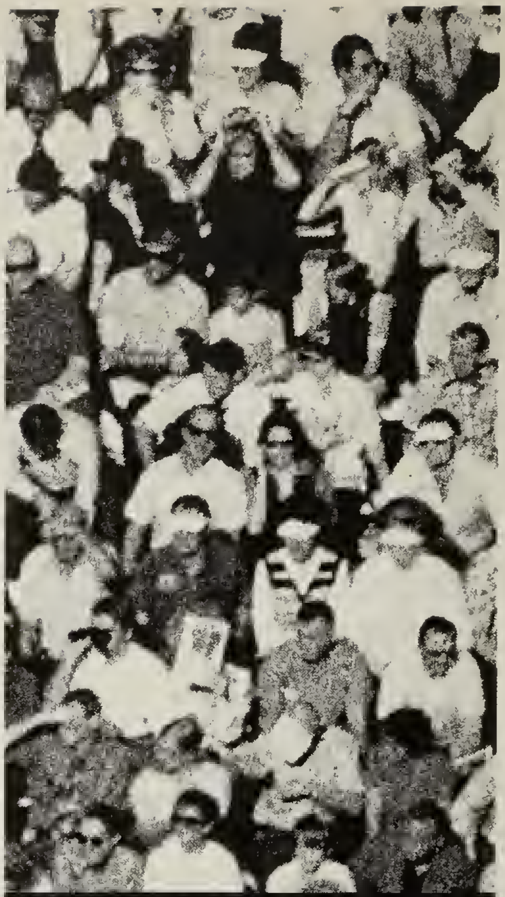
How Supplied

Motrin Tablets, 300 mg (white)	
Bottles of 60	NDC 0009-0733-01
Bottles of 500	NDC 0009-0733-02
Motrin Tablets, 400 mg (orange)	
Bottles of 60	NDC 0009-0750-01
Bottles of 500	NDC 0009-0750-02
Unit-dose package of 100	NDC 0009-0750-06
Unit of Use bottles of 120	NDC 0009-0750-26

Caution: Federal law prohibits dispensing without prescription.

NIM-3

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001



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NEW DIRECTIONS

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INSTRUCTIONS:

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   Mrs Morton Comess
   6565 North Forty Third Place
   Paradise Valley, Arizona 85253
2. Entries are limited to:
   Three per person .... Adults
   Two per person .... Youth (13 years through 17 years)
   Two per per person .... Child (12 years and under)
3. Deliver item or items ready for display, to the Safari Convention Center-Scottsdale, 9 a.m.—12 noon, Wednesday April 25, 1979
4. Items *must* be picked up between 2:30 p.m. and 3:30 p.m. on Friday, April 27,1979

REGISTRATION FORM:

I would like to enter the following items in the CREATIVE MOMENTS '79 to be held April 25—27, 1979 at the Scottsdale Safari Resort.

Describe in Detail	Exhibited Professionally	Kit	Own Design	Child	Youth	Adult

(One form per person please)

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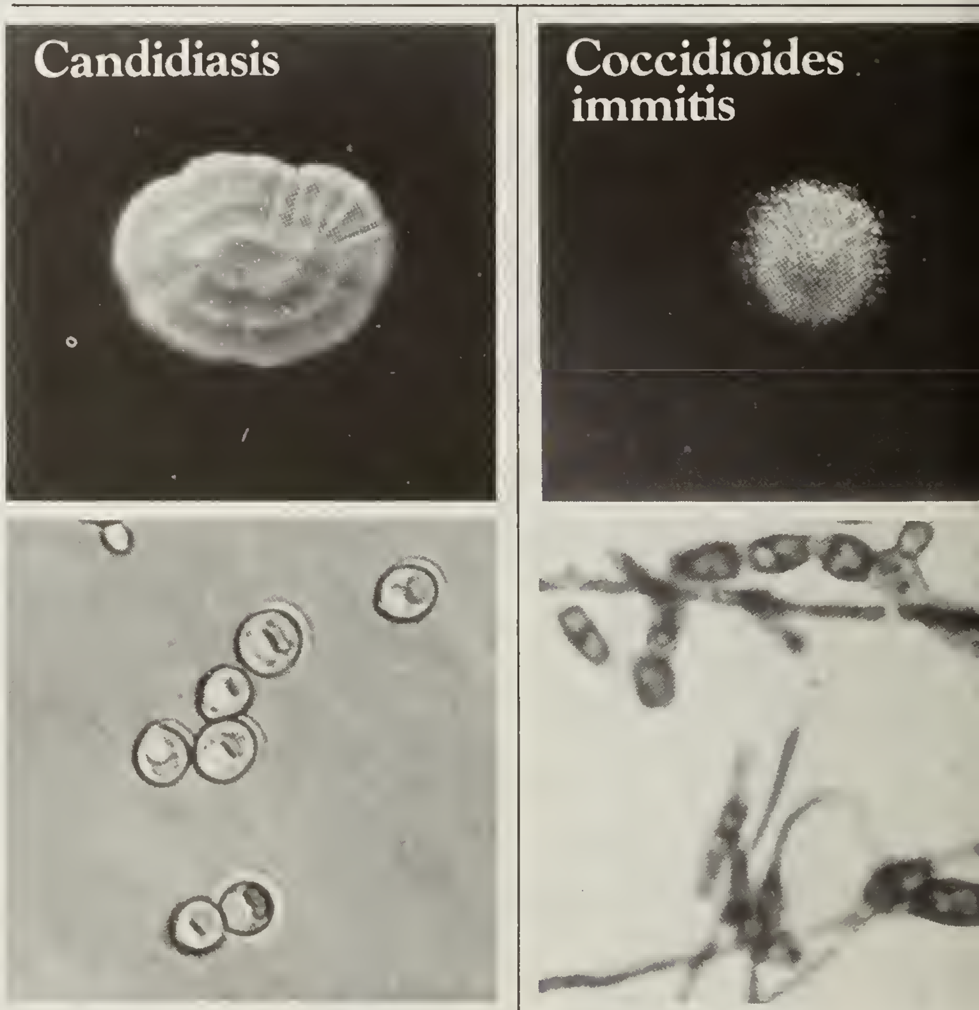
Efficacy of MONISTAT i.v. therapy...

highly favorable rates of recovery or clinical improvement

- effective against systemic candidiasis
  - chronic mucocutaneous candidiasis
  - coccidioidomycosis
  - cryptococcosis
  - paracoccidioidomycosis
- in patients who did not respond to amphotericin B therapy
- in immunologically-compromised patients with severe infections

rapid onset of clinical improvement
In most patients who responded, improvement was observed within 1-3 weeks of MONISTAT i.v. therapy; however, prolonged treatment courses may be necessary to prevent relapse.

no development of fungal resistance during therapy reported
In vitro resistance of clinical isolates has not been observed during clinical trials.



Photos courtesy of Dubos, J. R., Bacterial and Mycotic Infections of Man, J. B. Lippincott Company, 1968 and Burrows, W., Textbook of Microbiology, W. B. Saunders Company, 19th edition.

and the side effect profile

no nephrotoxicity or other permanent adverse effects in clinical studies

- even in prolonged therapy
- even in patients with renal disease

extensively evaluated
During clinical trials in over 400 patients, no permanent adverse reactions were reported.

Adverse reactions
MONISTAT i.v. should not be administered undiluted. Rapid injection of the undiluted solution may produce transient tachycardia or arrhythmia.

Adverse reactions include phlebitis, pruritus, rash, nausea, vomiting, febrile reactions, drowsiness, diarrhea, anorexia and flushes. Transient hematologic changes have occurred; therefore, the patient should be closely monitored.

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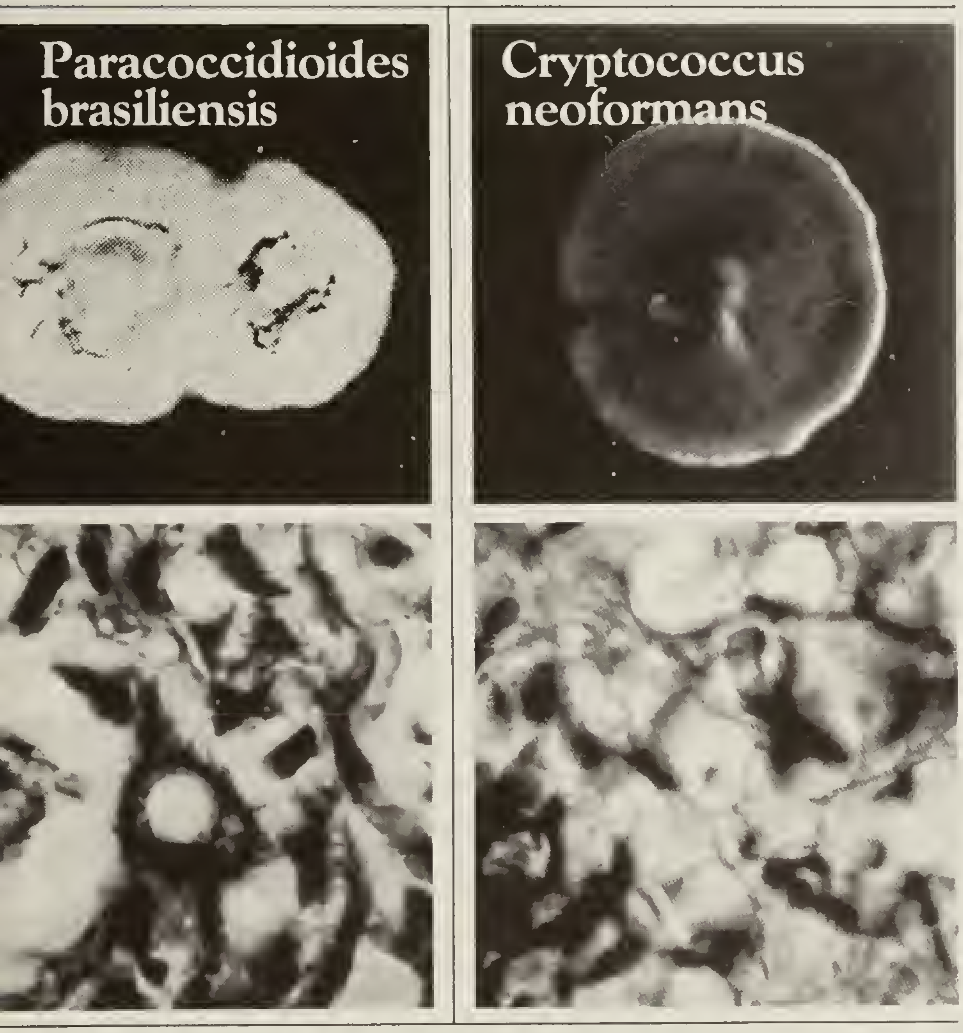
advancement systemic mycoses



generally well tolerated by severely debilitated patients

- cancer patients
- patients receiving immunosuppressive drugs
- patients with serious underlying conditions such as renal insufficiency or diabetes mellitus

for more information

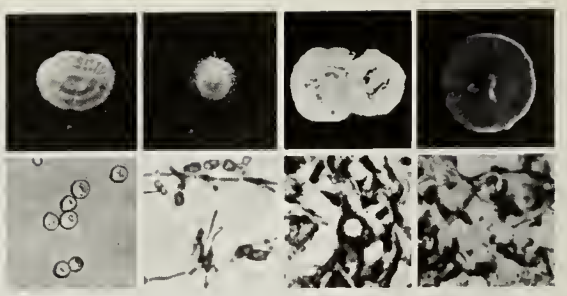
Because of the uniqueness of new MONISTAT i.v. only some of the highlights can be presented in this advertisement. For more information, i.e., product monograph, dosage schedules, etc., please fill out the coupon on the next page and mail to Ortho Pharmaceutical Corporation.

Please turn page for Prescribing Information

Ortho Pharmaceutical Corporation
Raritan, New Jersey 08869

new
Monistat i.v.
TRADEMARK
(miconazole)

broad-spectrum activity against major systemic fungal pathogens



in systemic fungal infections...

new Monistat i.v.

TRADEMARK

(miconazole)

a broad-spectrum systemic antifungal agent

DESCRIPTION: MONISTAT i.v. (miconazole) 1-{2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl) methoxyl ethyl} 1 H-imidazole is a synthetic antifungal supplied as a sterile solution for intravenous infusion. Each ml of this solution contains 10 mg of miconazole with 0.115 ml PEG 40 castor oil, 1.0 mg lactic acid USP, 0.5 mg methylparaben USP, 0.05 mg propylparaben USP in water for injection. Miconazole i.v. is a clear, colorless to slightly yellow solution having a pH of 3.7 to 5.7.

CLINICAL PHARMACOLOGY: MONISTAT i.v. is rapidly metabolized in the liver and about 14% to 22% of the administered dose is excreted in the urine, mainly as inactive metabolites. The pharmacokinetic profile fits a three-compartment open model with the following biologic half-life: 0.4, 2.1, and 24.1 hours for each phase respectively. The pharmacokinetic profile of MONISTAT i.v. is unaltered in patients with renal insufficiency, including those patients on hemodialysis. The in/vitro antifungal activity of MONISTAT i.v. is very broad. Clinical efficacy has been demonstrated in patients with the following species of fungi: *Coccidioides immitis, Candida albicans, Cryptococcus neoformans, and Paracoccidioides brasiliensis*.

Recommended doses of MONISTAT i.v. produce serum concentrations of drug which exceed the in-vitro MIC values for the fungal species noted above. Doses above 9 mg/kg of MONISTAT i.v. produce peak blood levels above 1μg/ml in most cases. The drug penetrates into joints.

INDICATIONS: MONISTAT i.v. is indicated for the treatment of the following severe systemic fungal infections: coccidioidomycosis, candidiasis, cryptococcosis, paracoccidioidomycosis, and for the treatment of chronic mucocutaneous candidiasis. However, in the treatment of fungal meningitis and urinary bladder infections an intravenous infusion alone is inadequate. It must be supplemented with intrathecal administration and bladder irrigation. Appropriate diagnostic procedures should be followed and MICs should be determined.

MONISTAT i.v. should not be used to treat common trivial forms of fungal diseases.

CONTRAINDICATIONS: MONISTAT i.v. is contraindicated in those patients who have shown hypersensitivity to it.

WARNINGS: Rapid injection of undiluted MONISTAT i.v., may produce transient tachycardia or arrhythmia.

PRECAUTIONS: Before a treatment course of MONISTAT i.v. is started, the physician should make sure that the patient is not hypersensitive to the drug product. MONISTAT i.v. should be given by intravenous infusion. The treatment should be started under stringent conditions of hospitalization but subsequently may be given to suitable patients under ambulatory conditions with close clinical monitoring. It is recommended that an initial dose of 200 mg be given with the physician in attendance. It is also recommended that clinical laboratory monitoring including hemoglobin, hematocrit, electrolytes and lipids be performed.

It should be borne in mind that systemic fungal mycoses may be complications of chronic underlying conditions which in themselves may require appropriate measures.

Pregnancy: Reproductive studies with MONISTAT i.v. in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus. There are no data, however, on the use of the drug in pregnant women.

Children: Since the safety of miconazole i.v. in children under one year of age has not been extensively studied, its benefits in this age group must be weighed against the possible risks involved.

ADVERSE REACTIONS: Adverse reactions which have been observed with MONISTAT i.v. therapy include phlebitis, pruritus, rash, nausea, vomiting, febrile reactions, drowsiness, diarrhea, anorexia and flushes. In the U.S. studies, 29% of 209 patients studied had phlebitis, 21% pruritus, 18% nausea, 10% fever and chills, 9% rash, and 7% emesis. Transient decreases in hematocrit and serum sodium values have been observed following infusion of MONISTAT i.v. Thrombocytopenia has also been reported. No serious renal or hepatic toxicity has been reported. If pruritus and skin rashes are severe, discontinuation of treatment may be necessary. Nausea and vomiting can be mitigated with antihistaminic or antiemetic drugs given prior to MONISTAT i.v. infusion, or by reducing the dose, slowing the rate of infusion, or avoiding administration at mealtime.

Aggregation of erythrocytes or rouleau formation on blood smears has been reported. Hyperlipemia has occurred in patients and is reported to be due to the vehicle. Cremophor EL (PEG 40 castor oil).

DRUG INTERACTIONS: Drugs containing cremophor-type vehicles are known to cause electrophoretic abnormalities of the lipoprotein. These effects are reversible upon discontinuation of treatment but are usually not an indication that treatment should be discontinued.

Interaction with the coumarin drugs resulting in an enhancement of the anticoagulant effect has also been reported. In cases of simultaneous treatment with MONISTAT i.v. and coumarin drugs, the anticoagulant effect should be carefully titrated since reductions of the anticoagulant doses may be indicated.

DOSAGE AND ADMINISTRATION

DOSAGE

Adults. The doses may vary with the diagnosis and with the infective agent, from 200 to 1200 mg per infusion. The following daily doses, which may be divided over 3 infusions, are recommended.

Organism	Dosage Range*	Duration of Successful Therapy (weeks)
Coccidioidomycosis:	1800 to 3600 mg per day	3 to > 20
Cryptococcosis:	1200 to 2400 mg per day	3 to > 12
Candidiasis:	600 to 1800 mg per day	1 to > 20
Paracoccidioidomycosis:	200 to 1200 mg per day	2 to > 16

*May be divided over 3 infusions.

Repeated courses may be necessitated by relapse or reinfection.

Children: A total daily dose of about 20 to 40 mg/kg is generally adequate. However, a dose of 15 mg/kg body weight per infusion should not be exceeded.

ADMINISTRATION: MONISTAT i.v. should be diluted in at least 200 ml of fluid. The diluent of choice is 0.9% sodium chloride or alternatively Dextrose 5% injectable solution. The intravenous infusion should be given over a period of 30 to 60 minutes.

Generally, treatment should be continued until all clinical and laboratory tests no longer indicate that active fungal infection is present. Inadequate periods of treatment may yield poor response and lead to early recurrence of clinical symptoms. The dosing intervals and sites and the duration of treatment vary from patient to patient and depend on the causative organism.

OTHER MODES OF ADMINISTRATION: Intrathecal. Administration of the undiluted injectable solution of MONISTAT i.v. by the various intrathecal routes (20 mg per dose) is indicated as an adjunct to intravenous treatment in fungal meningitis. Succeeding intrathecal injections may be alternated between lumbar, cervical, and cisternal punctures every 3 to 7 days. Bladder instillation of 200 mg of diluted solution is indicated in the treatment of mycoses of the urinary bladder.

HOW SUPPLIED: MONISTAT i.v. is supplied in 20 ml ampoules.

MONISTAT i.v. (miconazole) is an original product of Janssen Pharmaceutica N.V., Belgium, and co-developed by Ortho Pharmaceutical Corporation.

Ortho Pharmaceutical Corporation
Raritan, New Jersey 08869

Ortho Pharmaceutical Corporation
c/o 733 Summer Street
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AM2—79

Please send me more information on the new broad-spectrum, systemic antifungal agent... MONISTAT i.v. (miconazole).

____________________ M.D.

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Specialty____________________

October 1978

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Dean's Clinical Rounds

Rheumatoid Disease A Multiple Disciplinary Problem
Part II

Robert G. Volz, M.D.
John T. Boyer, M.D.
Eric P. Gall, M.D.
Michael J. Pitt, M.D.
Jack M. Layton, M.D.

Pathogenesis
John T. Boyer, M.D.

Rheumatoid disease is an inflammatory process of unknown etiology. An analysis of possible genetic factors suggests only a minor role while epidemiologic and immunologic studies point toward a viral etiology. Many scientists believe rheumatoid disease is caused by a foreign pathogen because it arouses so many features of the classical immune response and is modified by therapy which alters the immune and inflammatory systems.

The normal immune response to foreign material involves two major components of the lymphatic tissues: a cellular or T-cell response and a humoral or a B-cell response. The T-cell lymphocyte is derived from the thymus. These cells are capable through surface components of recognizing foreign material and of altering or destroying such antigens. An elaboration of small polypeptide molecules called lymphokines by T-cells further recruits and mobilized macrophages, eosinophils and polymorphonuclear cells.

The B-cell is derived from lymphatic tissue found within the small intestine. These cells respond through immunoglobulin surface receptors to foreign antigens by proliferating in number, and by differentiation into plasma cells. The proliferation of plasma cells provides for the elaboration of gamma globulin antibodies which are directed against foreign antigen. This antibody response is further amplified by activation of the complement system which occurs when sufficient antigen-antibody contact has taken place. This last step of the immune process is a powerful one as the mobilization of polymorphonuclears is provoked principally through the elaboration of complement factors and results in the phagocytosis of target antigens. It is the release of lysosomal enzymes from the polymorphonuclears that is at once both protective when destroying foreign material and harmful when destruction of surrounding tissues occurs.

This review of the immunologic response to foreign antigen also describes almost everything now known about the pathogenesis of rheumatoid disease except what the "antigen" might be. Rheumatoid synovial lymphocyte collections are known to contain both T- and B-cells. There is also observed within the synovium a remarkable proliferation of the plasma cell, a descendant of the B-cell. Gammaglobulins, and particularly rheumatoid factor (a gammaglobulin auto-antibody directed against a portion of other gammaglobulins), are also manufactured in the synovium. Lymphokines, the products of T-cell activation, have been identified in rheumatoid synovial fluid. The complement components of the synovial fluid are considerably reduced through activation and metabolism presumably provoked by rheumatoid immune complexes. Finally, the lysosomal enzymes of polymorphonuclears and, more importantly, the neutral proteases and collagenases have been identified in rheumatoid synovial fluids.

Clinical experiments further confirm the theory of an altered immunologic response as the pathogenesis of rheumatoid disease. Depletion of the T-cell population through continuous thoracic duct drainage for several weeks has invariably produced a remission in patients with rheumatoid disease. Unfortunately, this is short-lived. In the laboratory, lymphocytes taken from patients with rheumatoid disease can be provoked to a blastogenic response when cultured with fibroblasts, a finding not observed when lymphocytes are removed from normal patients. A modification of both the T- and B-cell systems with certain cytotoxic drugs frequently leads to a remission in rheumatoid arthritis. Decreasing the number of polymorphonuclears by such agents as nitrogen mustard also produces a remission. The future of improved therapeutic modalities for a patient who has rheumatoid disease will undoubtedly evolve from the evolution of further knowledge about the immunologic system.

Pathology
Jack M. Layton, M.D.

Rheumatoid arthritis is a systemic disease. A crippling of the patient is brought about by processes which affect the joints. The primary change is proliferation of the

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From: U of A Health Sciences Center, Tucson, AZ 85724. Reprint requests to Dr. Volz.

synovial membrane and of the perichondrium of the articular cartilage combined in many instances with a proliferation of the connective tissue and endosteum of the epiphyseal marrow directly beneath the cartilage. Proliferation of the synovial membrane produces a layer of granulation tissue which may extend over the joint cartilage as a pannus. Destruction and absorption of joint cartilage occurs at the point of contact with the granulation tissue pannus. Whenever a proliferation of the perichondrium takes place, it leads to the formation of a layer of specialized connective tissue which may be transformed into cartilage or bone. In addition, analogous changes may take place within the epiphyseal marrow of the bone itself. Atrophy of bone increases gradually. The joint is enlarged owing to thickening of the joint capsule and an increase in the amount of synovial membrane.

As a result of the progressive granulomatous reaction in the synovial membrane and articular connective tissues described above, joint cartilage and bone are *destroyed*, and supporting connective tissue structures are *deformed*. The joint destruction and deformity is usually proprotional to the intensity and duration of the active inflammatory process.

Although the lesions in rheumatoid disease involve both connective tissues and blood vessels, the vascular lesions have received less attention. Vasculitis, segmental of focal, is a hallmark of the disease. Arteritis and arteriolitis occur most often in advanced or highly active disease, involve vessels the size of digital arteries, and lead to degenerative and necrotic changes secondary to ischemia. But probably the most significant type of vascular involvement, also the least appreciated, is the venulitis and capillaritis. These segmental or confluent inflammatory lesions are prominent and clinically involve subcutaneous and synovial membrane tissue, especially during the early or rapidly progressive stage of development. Endothelial cells display hypertrophy and proliferation with numerous filopodia. Junctions between cells appear tight. Perivascular changes encompass separation of pericytes and alterations in the matrix of collagen. Lymphocytic and plasmacytic infiltrates follow. At the same time surface cells tend to lose cohesiveness, accumulate lysosomes and degenerate. Fibrinoid material accumulates among the surface cells. The entire thickness of the synovial membrane down to and into the ligamentous fiber bundles is involved.

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2. Reproduced with permission from Fritz, W.L., Paxinos, J., Gall, E.P. "Rational Use of New Nonsteroidal Anti-Inflammatory Drugs," *Drug Therapy* 8:36-61, 1978.
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Seminars in Endocrinology
and Metabolism

The Birth of Fiber and the Death of Fat

Stephen E. Dippe, M.D., F.A.C.P.
Jack E. Cook, M.D.

Editors:
Stephen E. Dippe, M.D.
Jerome Targovnik, M.D.

Most Americans like their meat to be marbled, of the highest grade, and quite juicy. We all seem to appreciate the smoothness and the delicacy given to the meat by the fat. The only problem is that fat can cause the cholesterol level to rise and cholesterol is a predominant risk factor for the development of heart disease.[1] However, encouraging data indicate Americans have already started to reduce the consumption of saturated fat.[2]

Recently, intriguing and valuable information indicates fiber may be an important substance for us to consume.[3] Fiber is thought to reduce the frequency of certain colon disorders.[4,5] The epidemiologic evidence seems to be the most convincing. The exact mechanism is unknown but may be due to factors such as changes in gastrointestinal transit time, increased stool bulk or effects on the bacterial content in the colon.[3,4] The consumption of fiber had been declining in America up until about 1960 after which it has remained steady.[6]

The reason these two particular food components are brought together in this paper is that fiber may also help lower the cholesterol level.[7] Thus, by increasing the fiber content of the diet and reducing the concentration of fat, particularly saturated fat, one then could affect the cholesterol level.

An area for physicians is trying to inform patients which foods to eat and not to eat. One means for determining the "safer" fat is by using the P/S ratio, which is nothing more than dividing the number of grams of polyunsaturated fat by the number of grams of saturated fat. For example, as noted in Table 1 below, cheese is a third fat and almost all that fat is saturated giving a very, very low P/S ratio. If we look at beef high

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From: Family Practice Center, Scottsdale Memorial Hospital, 7301 E. 4th St., Scottsdale, AZ 85251. Reprint requests: Stephen E. Dippe, M.D.

in fat, which usually represents the higher grade cuts of meat, the total amount of fat is also 30%, and the P/S ratio is a little more than that of cheese. As a result patients have been instructed to increase the consumption of turkey, chicken and fish because the total amount of fat is less. For example, in the light meat of chicken only 4% is of fat, and the P/S ratio is almost one. Thus, not only the concentration of fat is less, but the proportion of polyunsaturated fat is greater. This is not true of all birds, however. For example, ducks and geese have more fat and that fat is more saturated. Also, the dark meat of chicken contains more fat than the light meat. Fish have a P/S ratio that is very favorable. Also, the concentration of fat is considerably less in fish being about 1-2% with a few exceptions, like salmon, tuna and trout.

Also, it is important to note that the amount of fat found in many pork cuts have less fat than beef and it should be emphasized that the ratio of saturated fat and polyunsaturated fat also seems to be more favorable than that of beef. Finally, a word of caution concerning milk and milk products. It is important to emphasize that 2% fat milk only means that half of the fat is removed. Whole milk is about 4% fat. Nonfat milk is now available which contains no fat, is much lower in calories, and is high in protein. Skim milk is acceptable as it contains very little fat.

Table 1
FAT (ANIMAL PRODUCTS)[8]

Item	Total* (gm.)	Sat.[1] (gm.)	Pus.[2] (gm.)	P/S Ratio	Chol.[3] (mg.)
Cheese, American processed	31.60	19.98	0.95	.05	96
Cheese, Swiss	27.80	18.10	1.05	.06	93
Beef, high fat	29.30	12.70	0.83	.07	91
Beef bologna	29.20	11.90	0.90	.08	62
Beef frankfurters	29.10	11.20	1.20	.11	62
Cheese, mozarella (low fat)	16.10	10.07	0.45	.04	57
Beef, medium fat	16.20	6.80	0.60	.09	91
Veal, loin or rib	15.30	6.50	1.00	.15	99
Pork, loin or picnic	13.00	4.40	1.36	.31	88
Beef, lean	8.30	3.50	0.47	.13	91
Lamb; loin, leg or rib	7.60	3.20	0.44	.14	100
Eggs	11.50	3.16	1.91	.60	550
Pork, ham, lean	8.80	2.98	0.92	.31	88
Cheese, creamed cottage	4.50	2.85	0.14	.05	15
Tuna	6.80	2.27	2.10	.93	60
Chicken, dark meat	9.60	2.21	2.55	1.15	91
Salmon	9.90	2.18	2.69	1.23	60
Duck (raw)	8.20	1.91	0.92	.48	70
Turkey, dark meat	5.30	1.57	1.47	.94	101
Beef liver	3.70	1.50	0.73	.49	300
Chicken, light meat	4.30	1.18	1.10	.93	79
Trout	4.50	1.14	0.96	.84	60
Turkey, light meat	2.60	0.73	0.70	.96	77
Cheese, cottage (low fat)	1.00	0.51	0.02	.04	44
Flounder	1.20	0.28	0.49	1.75	60
Shrimp	1.40	0.20	0.55	2.75	150
Cod	0.73	0.12	0.27	2.25	50
Sardines	1.10	--	--		70

*Composition per 100 grams.
[1] Saturated Fat

*Composition per 100 grams.
[1] Saturated Fat
[2] Polyunsaturated Fat
[3] Cholesterol

Table 2
PLANT FIBER (FRUIT)[8]

Item	Total* (gm.)
Blackberries	5.0
Apples	3.4
Pear	2.4
Orange	2.1
Strawberries	2.1
Banana	1.8
Grapefruit	1.3
Peach	1.3
Cherries	1.2
Pineapple	1.0
Grapes	0.8

*Composition per 100 grams.

Table 3
PLANT FIBER (VEGETABLE)[8]

Item	Total* (gm.)
Broccoli	4.1
Carrots	3.7
Beans, string	3.4
Celery	3.0
Squash, summer	3.0
Cabbage	2.8
Beets	2.5
Radishes	2.2
Turnips	2.2
Onions	2.1
Cauliflower	1.8
Asparagus	1.7
Lettuce	1.5
Tomatoes	1.4

*Composition per 100 grams.

There is concern that insufficient protein intake will ensue if meat products are restricted. There are good vegetable sources for protein which do not have a high concentration of fat and have a more satisfactory P/S ratio. Many beans, for example, contain over 20% protein. Other non-meat sources, such as corn, oats, and other grains, have a high proportion of protein, up to 15%.[8] Of course, when whole grains are stripped of their protein sources, then the only starch is available.

Fiber is derived from plant sources. A very high concentration of plant fiber is found in 100% bran cereals where one third of the cereal is actually plant fiber. Products with over 10% fiber are pinto beans, rye flour, corn flakes, graham crackers, popcorn, and wheat cereals. Many other cereal products, breads, and starchy vegetables are excellent sources for fiber.[8] Lesser quantities of fiber, up to 5%, are found in a number of vegetable and fruit products as shown in Tables 2 and 3.

As far as we know, there are no ill effects from eating fiber and there are no ill effects from reducing the concentration of saturated fat. Therefore, it is important to suggest to your patients that good nutritional habits include reducing the total amount of fat and increasing the concentration of fiber in their diet. This will require ignoring adverse advertising that is presently bombarding our society. It will require patients and children to adhere to a diet high in vegetable products and lean products from animal sources. It will require the use of more natural products such as whole grain cereals, fresh fruits and vegetables. When processed or prepared foods are manufactured, saturated fat, sugar, salt, and artificial substances may be added and fiber may be removed.

It's too late to convince your patients to make these types of dietary changes, but it may not be too late for you to convince your patients to establish dietary habits in their children that promote better health.

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ACKNOWLEDGEMENT

Supported in part by the Edyth Bush Charitable Foundation.

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Seminars in Gastroenterology and Liver Disease

Diverticulosis — Diverticulitis:

Newer Concepts and Rare Case Presentation

Leon A. Rigberg, M.D.

Editors:
Leon Rigberg, M.D.
Stephen Glouberman, M.D.
George Burdick, M.D.

Diverticulosis affects approximately one out of three people over the age of 60. There is an increase in the incidence into the eighth and ninth decades and at that point, may involve two out of three people. Only a minority of these people will actually develop symptoms of diverticulitis and the complications. The most common location for diverticula is in the sigmoid colon. Diverticuli anatomically consist of a pouch of mucosa, which includes the mucosa and the muscularis mucosa, projecting through and beyond the circular muscles of the large intestine. Muscle thickening of both the circular and the longitudinal muscles, which are the taenia coli, are seen in most cases of diverticulosis. This same thickening has also been reported and seen in the individuals with the "irritable bowel syndrome." It is the increased muscle tone of the longitudinal muscles and the number of contractions of the circular muscles, which appear to cause shortening of the bowel and the so called "hypersegmentation." Each one of the segmented areas of the colon develops an increased pressure. This increase in manometric pressure would tend to produce a pulsion type of weakness in the area of the colon wall, in the region of penetration of a blood vessel, with resultant diverticular formation.

From: 6036 N. 19th Ave., Ste. 309, Phoenix, AZ 85015.

The most important complication of diverticulosis is diverticulitis. This is generally an inflammation involving primarily one, and not more than three or four diverticula in the same area. The inflammation present tends to affect the wall of the diverticulum and both proximal and distal portions of the colon itself. The peri colic and mesenteric fat areas are also involved. Microperforation of the diverticulum probably occurs more frequently than can be appreciated, but macroperforation results in peri colic abscess or local peritonitis or in other cases severe peritonitis. Fistula formation is common once abscess is present. Fistula into the bladder, vagina (more frequently seen in females with hysterectomy), and fistula into loops of small bowel, skin and rectum have been reported. Septicemia with positive blood cultures has been reported and when associated with diverticulitis, multiple antibiotic therapy is the treatment of choice. In every case of diverticulitis, multiple blood cultures appear to be indicated. The use of antibiotics should be parenteral as opposed to oral. Antibiotic therapy is aimed at both aerobic and anaerobic agents. Other complications of diverticulitis besides perforation, abscess and fistula formation, are that of obstruction and hemorrhage. Originally, carcinoma of the colon was felt to be more common in individuals with diverticulitis, however, this has not been found to be true.

A very unusual complication of diverticulitis, septic meningitis was recently seen in an 89-year-old woman. She presented with an upper respiratory infection for five days prior to coming to the hospital. And had progressive stiffness of her neck and fever. In addition she had a history of chronic constipation, mild abdominal discomfort but no previous history of intestinal surgery, diarrhea, hematemesis or melena. She also had a history of taking Lanoxin daily for congestive heart failure and had a history of mild chronic obstructive pulmonary disease.

In the emergency room, she had nuchal rigidity, was confused, dehydrated and unable to respond to verbal commands. Deep tendon reflexes were diminished and Babinski's sign bilaterally was negative. The rest of the exam was unrevealing.

Cloudy cerebral spinal fluid was obtained which demonstrated 1,200 WBCS, 800 RBCS, 88% PMN, 12% lymphs and had 446 mg/dl protein, 23 mg/dl glucose, and a chloride of 104 MEG/L. Opening pressure was approximately 150 cm/H_2O. She had a peripheral white blood count of 18,000 (88% PMN) and a serum glucose of 231 mg/dl.

The patient was initially treated with high doses of intravenous penicillin, for possible pneumococcal meningitis although a gram stain of CSF demonstrated, what was thought to be gram negative cocci. CSF culture at 48 hr. was positive for E. coli. Blood cultures also were positive for E. coli. The patient's antibiotic therapy was changed from Pencillin to Ampicillin, and within eight days she was clinically improved.

When she became more alert, she told of left lower quadrant discomfort and a weight loss of five pounds during the preceeding six months.

Because the source of the E. coli was unclear and her history pointed to a possible gastrointestinal origin a barium enema was obtained. This demonstrated marked deformity of the sigmoid colon, a fistula formation, pericolic abscess and stricture.

To further evaluate the colon, left sided colonoscopy was performed which demonstrated colonic stenosis at 25 cm., with marked irritability, and spasticity. A marked degree of inflammation was present in the region of the fistula seen on barium enema exam.

Two weeks following admission she underwent surgery for possible colon resection or drainage of her abscess. At the time of surgery, a 19 cm. by 3.2 cm. in diameter segment of colon was removed which revealed acute and chronic diverticulitis with peridiverticulitis, abscess formation.

In the management and treatment of diverticular disease, earlier surgical intervention in the individual who has had two or more attacks of documented diverticulitis with left lower quadrant pain is now suggested. In these individuals, either a one stage or two stage resection may be indicated on an elective basis. Surgery also has its place now in individuals who have had one attack with evidence of perforation, with diverticulitis and obstruction, diverticulitis and fistula formation, diverticulitis and severe hemorrhage uncontrolled by medical measures, and probably the individual who has severe diverticular disease with symptoms younger than age 50.

The medical management of diverticular disease, is that of high fiber diet to increase stool bulk, and the use of supplemental unprocessed bran, Hydrophilic colloids — Psyllium hydro-philic mucoloid, and possibly the use of stool softeners. It should be known that no specific regimen has been proven to alter the natural history of diverticulosis or to prevent its complications. This particular fiber diet program is utilized in the "irritable bowel" patients, as well as in diverticulosis in an attempt to lower the pressure in the segments of the colon and to relieve lower abdominal pains and promote more regularity.

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Neurology

Vascular Headache Treatment Update

G. Scott Tyler, M.D.
Harold E. McNeely, Ph.D.
M. Lawrence Dick, R.Ph., M.S.

Editors:
Betty F. Ball, M.D.
Barry Hendlin, M.D.
Lawrence Z. Stern, M.D.

Interval (prophylactic) treatment of vascular headache has been facilitated in recent years by the discovery that medications intended for use in other conditions are effective for the headache problem. Treatment methods commonly advocated are outlined and personal observations from random case study by the authors are made.

By definition vascular headaches[1] result from changes in tone of the scalp vasculature leading to local pain which is often unilateral and often at least in part nocturnal. There are usually systemic symptoms, most commonly nausea and vomiting. It is our opinion that the term migraine is to be avoided as this term is too broadly used to mean any type of severe head pain. The only exceptions to the use of the term migraine are where it is modified by such terms as menopausal, hemiplegic, ophthalmoplegic, common, classical, etc.

The first step in treatment is a correct diagnosis. The initial diagnostic effort is best directed toward verifying that the recent attacks are the first of the patient's life. The current headache may be of such severity as to augment the patient's neurotic tendencies to "forget" to inform the physician of prior attacks until specifically questioned. In the patient with menopausal migraine it is almost always necessary to probe pointedly for a history of "sick headaches" as a teenager, but such a history is almost always obtainable. Once the physician is satisfied that the problem is indeed of recent origin, further obstacles arise.

TABLE 1
A GRADED LIST OF CHARACTERISTICS
OF VASCULAR HEADACHE
And Precautions Against Misdiagnosis

CHARACTERISTICS OF VASCULAR HEADACHES IN GENERAL	
Vomiting (when no medication taken beforehand)	+8
Hemicranial (one sided pain)	+4
Nocturnal onset at least part of the time	+4
Patient has been to ED or office for narcotic injections	+3
Headache occurs only with menstruation	+3
Definite free intervals between headaches	+2
Headache relieved by ergotamine derivative	+2
Marked decrease in headache with pregnancy	+2
Headache more than rarely incapacitating	+1
Nausea (without vomiting) (when no medication taken beforehand	+1
Headache more frequent with menstruation	+1
Photophobia and/or acoustophobia with headache	+1
Throbbing pain early in headache	+1
Cyclic vomiting as a child	+1
Relief of headache given by pressure on temporalis artery	+1
Family history of unilateral, nocturnal headache with vomiting	+1
Electroencephalogram nonspecifically abnormal	+1
ADDITIONAL CHARACTERISTICS OF CLASSIC MIGRAINE	
Visual prodrome (if prodrome sensory, mood change or other, value drops to 8 points)	+10
ADDITIONAL CHARACTERISTICS OF CLASSIC MIGRAINE	
Clustering of headaches	+3
Vasomotor phenomena (ipsilateral nasal obstruction and eye redness)	+4
Headache precipitated by alcoholic beverage	+2
History of gastric ulcer	+2
Female sex (with other characteristics of migrainous neuralgia)	—10
PRECAUTION AGAINST DIAGNOSING VASCULAR HEADACHE IN OLDER WOMEN	
Woman of age greater than 55 years and off estrogens and with no hot flashes for better than two years	—8
PRECAUTION AGAINST MISDIAGNOSIS OF HEADACHE SECONDARY TO CERVICAL ARTHRITIS[3]	
Older patient who obtains relief of nocturnal headache by sleeping in a recliner chair	—8
PRECAUTION AGAINST MISDIAGNOSIS OF HYPERVENTILATION HEADACHE	
In a patient less than 30 years substract 2 points for each of the following that are present early in the headache: dyspnea, palpitations, dissociation, dryness of mouth, sighing or yawning, weakness or tiredness	—up to 12

Twelve or more points brings the diagnosis to the 98% level of confidence and 10 points to the 75% level.

One encumberance to the correct diagnosis of the first few headaches is the absence of a sufficient number of headache episodes to form a recognizable pattern. It is necessary in such a patient to secure the diagnosis against the presence of space occupying lesions (tumors, pseudo-

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From: Headache Group of the Southwest, 1402 N. Miller Rd., Scottsdale, AZ 85257. (Drs. Tyler and McNeely). Pharmacy, Phoenix Memorial Hospital, P.O. Box 21207, Phoenix, AZ 85036. (Mr. Dick).

TABLE 2
DRUGS AND THEIR DOSAGE USED IN PREVENTION OF VASCULAR HEADACHE

cryproheptadine (Periactin)[5]	8 mgm qid
propranolol (Inderal)[6]	40 mgm qid
tricyclics (e.g., Elavil)[7]	75 mgm hs
methysergide (Sansert)	2 mgm tid
phenytoin (Dilantin)[8]	300 mgm daily

Dosage is that commonly found effective for adults by the author. Order of listing is that of probable effectiveness weighed against side effects. Except for methysergide, initial dosage is usually lower and ultimate effective dosage may be higher.

tumor, vascular malformation, aneurysm, etc.), impairment of general health and intoxications (hyper- and hypothyroidism, polycythemia, carbon monoxide exposure, anemia, hepatic and renal disease, etc.), diseases of the nasal sinuses (infection, polyps, etc.), and dental conditions (infection, impaction, occlusal difficulties,[2] etc.). Of even more difficulty is the recognition in the older patient of the periodic vascular headache sequestered among constant muscle contraction headache which may be complicated by depression, cervical arthritis[3] and/or dental occlusal problems. A tabulation of vascular headache characteristics with a grading system (Table 1), when adapted to one's own precepts and prerogatives, may be useful. (See also Stead, et al[4]).

The use of the various ergot preparations in their variety of routes of administration is probably best limited to patients with infrequent, largely diurnal headache with a reliable prodrome. Under other circumstances there are too many excellent preventative medications available to warrant the more than occasional use of ergotamines. Use of ergotamines nearly always leads to the patient administering the medication when he or she thinks or fears headache is about to occur. This leads to abuse of the preparation; certainly the ergotamines should not be used as an analgesic.

Table 2 lists the prophylactic medications most likely to be effective with their optimal (but not necessarily initial) dose. The scientific basis for the use of any of these, except possibly methysergide, is virtually non-existent. These medications probably all work to prevent the reaction: platelet-serotonin $\underset{\longrightarrow}{\text{(histiocytes)}}$kinin$\longrightarrow$vasodilation$\longrightarrow$ pain. They possibly work as serotonin blockers (methysergide, cyproheptadine, propranolol, tricyclics), as membrane stabilizers (phenytoin), or on the nerves regulating the blood vessels (propranolol).

Methysergide and cyproheptadine are clinically interchangable in effectiveness, i.e., a patient who responds to one will almost always respond favorably to the other, leaving one to choose between the drugs relative to their side effects. The tricyclics are particularly helpful in the combined vascular and muscle contraction headache of middle life. The patient's usual acute-attack treatment with ergotamines and analgesics is to be continued during initiation of prophylactic treatment.

Medications other than those listed in the table have been advocated in the treatment of vascular headache. These include Midrin, a combination agent containing isometheptene as a substitute for ergotamine, acetaminophen, and the sedative dichloralphenazone as a substitute for pentobarbital, used in acute treatment. Papaverine[9] and clonidine[10] (Catapes) have been noted by some to be effective but have never become popular. Histamine desensitization, and, in desperation, adrenal corticosteroids[11] are still useful on occasion in migrainous neuralgia. Lithium,[12] carefully regulated as always by blood level, is reported as useful in migrainous neuralgia. The monoamine oxidase inhibitors[13] are useful, again in desperation, in common and classic migraine. The most recent approach is the use of any of the platelet agglutination inhibitors[14] including regular use of aspirin.

In the occasional patient who requests non-medicinal relief of the vascular headaches the following may be tried: diet[15] is particularly effective in migrainous neuralgia which is almost invariably decreased with the avoidance of tyramine or phenylethylamine containing foods such as alcoholic beverages and chocolate. Sphenopalatine ganglia block is useful and inhalation of high concentrations of oxygen has been advocated in migrainous neuralgia. Biofeedback for vascular headache may be useful in selected patients.

The effort required for diagnosis and medication of vascular headache is exceeded only by the struggle to mobilize and to maintain the pyschic energy of the chronic pain sufferer which will permit them to follow a sometimes complex treatment program.

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Non-Invasive Scanning Techniques for Gynecologic Cancer

Charles H. Nash, III, M.D.
David S. Alberts, M.D.

Editor:
David Alberts, M.D.

Errata:
This article originally appeared in Arizona Medicine. Vol. 35, Page 732. Because of printing errors the article is being re-published in its proper sequence.

A major problem in the management of gynecologic malignancy is the difficulty of early identification and subsequent measurement of pelvic tumors. Once treatment is initiated, there are relatively few non-invasive diagnostic tools available to objectively quantitate change in tumor size, and physical examination may frequently be misleading. This report summarizes the status of several non-invasive scanning techniques used for evaluating pelvic tumor masses at the University of Arizona and other medical centers.

Pelvic Ultrasonography

Since the early 1960's pelvic ultrasonography has been a valuable test routinely employed for both obstetrical and gynecologic diagnosis. It has the advantages of being rapid, accurate, and relatively inexpensive. Obstetricians have used it to determine fetal gestational age, screen for birth defects, and study pelvic anatomy. The B-mode sonogram can also accurately detect pelvic tumors, and with serial measurements it can be used to follow the progress of tumors in response to surgery, radiation therapy, and chemotherapy. The consistency of a mass (i.e., the solid, semi-solid, or cystic nature) can be determined, and relatively precise measurements can be made directly from the sonogram. The sonogram can identify pelvic or retroperitoneal lymphadenopathy, as well as hepatic, splenic, or intra-renal masses.

There are a few problems in obtaining a high-quality sonogram, however. A full urinary bladder is necessary to assure an accurate study and to localize masses or anatomic structures. When urinary incontinence is a problem, a temporary catheter can be used to fill the bladder. Also, sonograms are frequently difficult to interpret in patients with extensive adhesions or bowel gas

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From: The Section of Hematology and Oncology, Department of Internal Medicine, University of Arizona Health Sciences Center, Tucson, Arizona 85724.

because multiple echo densities will be seen.

Currently at the University of Arizona we perform B-mode sonograms of the abdomen and pelvis with gray-scale imaging techniques in longitudinal and transverse directions. A typical scan takes about 30-45 minutes to perform. With the baseline or pretreatment scan, masses are localized and their size is recorded; thereafter, sonograms are obtained serially to evaluate changes in tumor size following chemotherapy or radiation therapy. The performance of directed biopsy of pelvic masses under sonographic guidance may increase the safety of this procedure. For patients with inconclusive sonogram results other procedures are now available.

Cobalt-57-Bleomycin Scanning

Newer radiopharmaceutical agents have added another dimension to the non-invasive evaluation of gynecologic tumor masses.[3,4] These agents are tumor specific (i.e., they are selectively taken up by tumors). Cobalt-57-labeled bleomycin is one such radiopharmaceutical now available for tumor scanning.[7,9] One to 1.5 millicuries of Co^{57}-bleomycin is administered intravenously, and scanning is performed after 6, 24, and 48 hours. Since the radionuclide is immediately taken up by the kidneys, bladder wall, and liver, the best tumor imaging is achieved at 48 hours when tumor-to-plasma ratios are highest and most of the radionuclide has been excreted into the urine. To date, there is not enough experience with this scanning technique to determine its role specifically for the localization and measurement of gynecologic tumors; however, we are currently evaluating this at the University of Arizona Cancer Center in a study comparing the efficacy of Co^{57}-bleomycin and ultrasonography for pelvic tumor evaluation.

Computed Tomography Scanning

The increasing availability, precision, and accuracy of computed tomography (CT) scanning makes this a potentially important non-invasive diagnostic technique for the measurement of gynecologic tumor masses.[5,6,8] The indications for and cost-effectiveness of this procedure are still under investigation.[2] Scans are performed at the University of Arizona with a third-generation CT scanner which is able to scan a body slice in 4.8 seconds, thus eliminating movement artifact due to breathing and peristalsis. Oral Gastrographin® and intravenous Renographin® are used to outline the gastrointestinal and urinary tracts, respectively. A high-quality scan requires 1-2 hours, during which the patient must be relatively motionless. Measurements of tumor size can be readily made with this technique, and, as with sonography, directed biopsies can be performed with CT control to assure biopsy of the correct structure.

Discussion

The decision regarding which test to use to follow the course of cancer in a given patient must be made on an individual basis. Alberts et. al.[1] found that radionuclide scanning with indium-111-bleomycin and pelvic sonography were complementary procedures for evaluating pelvic tumors in patients with endometrial and ovarian carcinoma. The combination of these procedures yielded a high degree of accuracy in surgically confirmed cases. It was suggested that both ultrasound and In ^{111}-bleomycin scanning be used for initial diagnosis. Then, if the sonogram adequately depicted the tumor present, it alone could be used to follow the patient. If the sonogram was inadequate the In^{111}-bleomycin scan could be used for follow-up tumor evaluation.

We have recently carried out a prospective study to compare sonography with CT scanning to identify and measure gynecologic tumors.[5] In 15 patients with surgical documentation of tumor size and location, the combination of CT and sonography accurately measured disease in all cases. There were two false negative sonograms and two false negative CT scans. There were no false positive scans in the study. We concluded that sonography is as accurate as CT scanning in the measurement of gynecologic tumors.

Considering the cost of a CT scan (which is roughly four times as expensive as a comparable sonogram) and the time requirement, we believe the B-mode ultrasound to be the more efficacious technique for serial tumor measurement. The combination of tests can provide added diagnostic confidence, particularly when the clinician suspects tumor but the initial scanning procedure is inconclusive or negative. Another interesting finding is that the CT scan appears to be more accurate in defining uterine wall pathology, whereas the sonogram is useful mainly for defining uterine size and contour. We plan to use the sonogram as the initial test for patients with gynecologic cancer, although newer techniques, such as Co^{57}-bleomycin whole body scanning, are being studied.

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Pause

William B. McGrath, M.D.

There has been a surf of articles and books on transitions or phases in the course of human being. Infancy, childhood and adolescence have had long and scholarly attention. More recently dying and bereavement were in wideangle view. And now one reads everywhere about the stages of adult life.

Some of these concerns are almost faddist in their swift dissemination. Overly popularized, they break and recede like waves at the shore.

Never to be forgotten, however, is the value of rites of passage. They had their origins and have their continuance in the misty, intermediate zone between preliterate gestures and the cognitive processes of language. Rituals are rather like habits. They allow the disengagement of conscious and effortful selecting of words, as in conversation or rhetoric or in one's silent soliloques. Meanwhile a rite or ritual gives venting expression to experiences of such joy or anguish or solemnity as cannot be put into words or otherwise shared.

Blessed indeed are baptism and confirmation or bar mitzvah, graduation exercises and costumes, engagement festivities and marriage ceremonies, farewell parties, prewar rallies and ticker tape celebrations of peace, wakes and funerals.

Those who become cynical and scoff at participation in such rites estrange and spiritually ostracize themselves. Neglecting the atavistic, tribal sense of community they lose all concept and feeling of the brotherhood of man. Witness the alien and brutal attitudes of terrorists who attack their own human kind.

Thank God, in contrast, for service clubs like Rotary or Kiwanis with their stereotyped but wonderfully significant rituals.

Momentous changes and methods of adapting to them are pressing concerns of many institutions and many thoughful individuals.

No less important are the smaller, narrower "passages" of the person in everyday life. For economy of space we'll put it dogmatically: Whenever one is changing his role, his psychological uniform, he should "pause for identification," and the pause, however brief, should include a bit of ritual.

When, for example, a business or professional man too abruptly relinquishes his public persona to recapture that of his private or hearthside self, he has allowed no time or place for adjustment. He will have dragged the day's worries and frustrations on into the evening, contaminating himself and an atmosphere which should be harmonious and refreshing. Needless to say, intermittent stress is not nearly so harmful to the individual (and to his family!) as stress which is unremitting.

As others have remarked, we spend a lot of our time in waiting.* The child is waiting to become an adult. The medical student looks forward to being a physician. The youth is hoping to become self-supporting or engaged or married. The old person is waiting to die.

Again, in the smaller, more intimate areas of our concern one waits for a day off or a vacation or waits for an elevator or is delayed in traffic.

Instinctively and without thinking why, people use various practices in easing the transitions of ordinary life. Lawyers used to congregate in a tavern after work and josh with their colleagues, decompressing. Some business folk will habitually meander through a park, enjoying the shrubs and flowers. (I find fault with newer cities which do not plan parks where they are most needed, in middle class and affluent neighborhoods.) A friend visits briefly in a church, seeking repose and readjusting his perspective. Others go to a gymnasium or play racquet ball or jog. Meditation, practiced regularly and ritualistically, can be surprisingly beneficial. The mantra is devoid of meaning and therefore not associated to worries or resentments or regrets. Dwelling on it closes the door to all or nearly all organized cognition. Meditation provides an interlude in which the mind can return part way to a restful state like that which we sometimes observe in contented and timeless animals. We lost that paradise with the developing of language and with our ceaseless thinking.

Our puritan ethic (cliche) inclines us to associate waiting to idleness, to unproductiveness and waste. No; the time spent in transitions, in changing clothes, so to speak, should be richly full and just as cherished as our work. In some strange and simmering way, intervals of waiting or changing release the inspirational and creative functions of the mind.

From: Camelback Hospital, 5051 N. 34th Street, Phoenix, AZ 85014.

*Acknowledgement: A very small part of this article was stimulated by "The Semantics of Transitional Space" by Christine Nystrom, Executive Editor of the General Semantics magazine, ETC.

Renal Disease

Naproxen Nephrotoxicity

Karen C. Cartwright, M.D.
Tracy L. Trotter, M.D.
Melvin L. Cohen, M.D.

Editors:
Georgetta C. Bidwell, M.D.
George Nickas, M.D.

Abstract

A case of interstitial nephritis is presented associated with the use of naproxen in the treatment of rheumatoid arthritis. Azotemia and minimal urinary findings occurred after three months of naproxen therapy, and quickly disappeared following its discontinuation. Biopsy evidence is presented.

Naproxen, one of the newer nonsteroidal anti-inflammatory drugs, has been shown in many studies to be an effective antiarthritic and analgesic. It has been found useful in rheumatoid arthritis, degenerative joint disease and possibly gout. Published data suggest that in rheumatoid arthritis naproxen is comparable to moderate doses or aspirin or indomethacin.[1,4] Analgesic efficacy has been shown in patients with moderate postoperative pain following orthopedic, dental or other surgical procedures and in postpartum uterine pain.[5,6]

We are presenting a case of an adolescent boy who developed interstitial nephritis and azotemia associated with naproxen. We believe this is the first report of this complication.

From: Department of Pediatrics, St. Joseph's Hospital and Medical Center, 350 W. Thomas Road, Phoenix, AZ 85013.

Case Report: H. B., a caucasion boy (B.D. 1-20-59), was in good health until 8-5-74 when at the age of 15 8/12 years he presented with generalized stiffness of his extremities. This progressed rapidly to frank arthritis involving his hands, wrists, ankles, knees, feet, shoulders and neck. From August 1974 until January 1975 he was treated by his local medical doctor with 10 grains of aspirin three times daily and 15 mgs. of "cortisone" daily. In January 1975 he was admitted to Arizona Children's Hospital for uncontrolled arthritis. His weight on admission was 55.5 kilograms. Examination at that time revealed moderately severe synovitis of the proximal interphalangeal, metacarpophalangeal, wrist, elbow, shoulder, ankle, and knee joints. His neck and hips were most symptomatic. Laboratory tests revealed a hemoglobin of 14.4 gms/dl, erythrocyte sedimentation rate 25, urinalysis normal, urine culture negative, rheumatoid factor negative, anti-nuclear antibody negative, serum iron 70 mg/dl, EKG normal, chest x-ray normal, and a slightly increased gamma globulin on a serum protein electrophoresis. The diagnosis on admission was polyarticular rheumatoid arthritis.

The steroid was discontinued and the patient was begun on aspirin, magnesium-aluminum hydroxide (Ascriptin R) 600 mg. every 6 hours and aurothioglucose (Solganol R) 50 mg. I.M. every week, as well as physical therapy. By June 1975 he received a total dose of 800 mg. of gold and had shown no improvement. Examination was unchanged. A salicylate level was 3.3 mg.%. He was also noted to have a generalized macular rash which was thought to be secondary to gold therapy. At that time the gold was discontinued and the aspirin was continued with emphasis on compliance. He was also started on prednisone 5 mg. every day.

He was seen every 6 to 8 weeks over the next 6 months with only slight improvement. He was then lost to follow-up for one year, but when next seen at Arizona Children's Hospital in September, 1976 his arthritis had evolved into severe rheumatoid arthritis with generalized synovitis involving all of the small joints, and rheumatoid nodules appeared over the extensor surface of his forearms. He had stopped the prednisone on his own 5 months previously.

He was continued on aspirin 600 mg. every 6 hours and was started on naproxen 250 mg. twice daily. He continued on the naproxen until December 9, 1976 when he was admitted to Arizona Children's Hospital with persistent arthritis, anorexia, pallor, right cervical and submaxillary adenopathy and moderate splenomegaly. The aspirin was continued but the naproxen was stopped. His hemoglubin was 6.3 gm/dl and his WBC 8100/cu mm with 68% segs, 8% bands, and 24% lymphs. A reticulocyte count was 1%, sedimentation rate 66 mm, monospot negative, ANA negative, LE prep negative, TB and coccidiomycosis skin tests negative, platelet count 132,000/cu mm, BUN 67 mg/dl and creatinine 4.5 mg/dl. An intravenous pyelogram at that time revealed moderately large kidneys bilaterally with no evidence of obstruction. On December 12, 1976 the aspirin was discontinued. On December 14, 1976 he was transferred to St. Joseph's Hospital in Phoenix for evaluation of his renal failure and for evaluation of a possible malignancy. At the time of transfer his creatinine was 4.8 mg/dl, BUN 67 mg/dl and hemoglobin 6.6 gm/dl. A urine contained 1+ protein, no glucose, 10 to 20 WBC's, a trace of blood, an occasional rbc and a few granular casts. On the night of admission he was transfused with 1 unit of red blood cells and the following day he underwent a right percutaneous renal biopsy. His serum creatinine on 12-15-76 (3 days after naproxen was discontinued) was 2.8 mg/dl and a BUN was 43 mg/dl. A bone marrow and submaxillary salivary gland biopsy were both normal. A cervical node biopsy revealed nodular sclerosing Hodgkin's lymphoma. On 12-17-76 a creatinine was 2.1 mg/dl at which time he was started on chemotherapy. The nephropathy was considered to be toxic in origin and no therapy was instituted. Follow-up creatinine was 1.1 mg/dl twelve days after discontinuing the naproxen, 0.9 mg/dl a week later, and long term follow-up 0.7 mg/dl consistently.

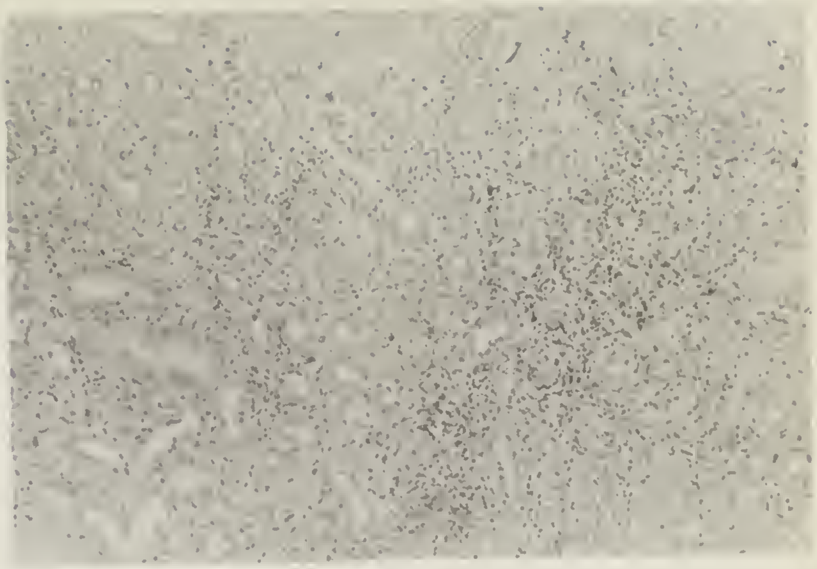

FIGURE 1
Prominent mononuclear interstitial infiltrate, tubuler atrophy and normal glomerulus. H & E x 400.

Biopsy Results:

Light microscope demonstrated a favorable core of renal cortex containing twenty-one glomeruli. The major alterations were focal areas of prominent mononuclear interstitial infiltrate with some corresponding increase in fibrous tissue and tubular atrophy. Also observed were occasional focal glomerular mesangial hypercellularity and increase in mesangial matrix. Most glomeruli however appeared normal. (Fig. 1). Blood vessels were also normal. Electron microscopy confirmed the minimal mesangial changes and showed varying amounts of intersitital collagen fibers, large numbers of lymphocytes, some plasma cells and histiocytes. Although there was some focal thickening of the glomerular capillary basement membranes, most basement membranes were normal. There were no electron dense deposits. (Fig. 2). Immunofluorescent microscopy revealed no deposition of IgG, IgM, IgA, C_3, C_4 or fibrin.

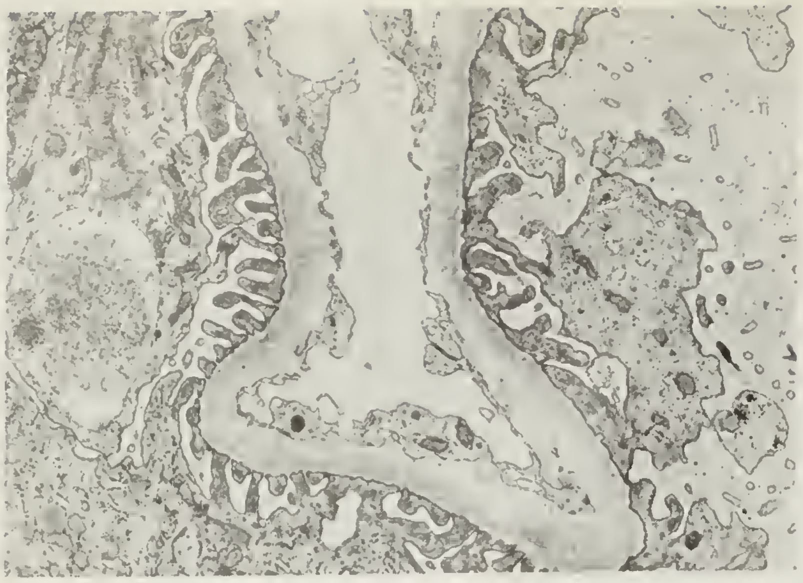

FIGURE 2
Normal basement membrane and surrounding structures. Original magnification x 21,000, reduced by 60%.

Discussion:

The incidence of side effects with naproxen has been low, with various reports estimating their occurrence in up to 15 percent of patients.[3] Adverse reations appear to occur less frequently than with aspirin or indomethacin.[7,8] Most investigators have found upper gastrointestinal complaints to be most frequent, commonly abdominal discomfort, indigestion, nausea and vomiting. Central nervous system side effects such as headache, vertigo, lightheadedness and drowsiness have also been seen and in some therapeutic trials have occurred more frequently than gastrointestinal symptoms.[1] More rarely skin rashes and ecchymosis have been attributed to naproxen.[3] Gastrointestinal bleeding has been seen and fatal hemorrhage was reported in 4 cases by Cuthbert.[9] Jaundice was described in two patients, one of whom appeared to have the cholestatic form.[10] The other had a clinical picture suggesting a drug induced hepatitis.[11] Both patients had complete recovery of liver function after discontinuing the drug.

A review of the English literature showed no previous report of renal complications associated with the use of naproxen in humans. Animal studies by Hallesy, et. al. did find kidney changes in mice when given doses 10.4 to 41.7 times higher than recommended human doses.[12] These changes were not seen in studies with other animals. The pathologic lesion is described as being similar to that found in analgesic nephropathy and reported with other nonsteroidal anti-inflammatory drugs. The changes are those of papillary necrosis, frequently in association with a secondary chronic interstitial nephritis.

There seems little doubt that naproxen was the causative agent in the interstitial nephritis and renal insufficiency reported here. Other considerations however included gold and analgesic nephropathy, Sjogren's disease, and the interstitial nephritis of rheumatoid arthritis. Gold nephropathy is generally manifested by heavy proteinuria with or without the nephrotic syndrome.[13] Gold inclusions may be found[14] and occasional electron dense depositis are found in the glomerular basement membranes by electron microscopy.[15] Analgesic nephropathy, most often phenacetin related, with or without aspirin, presents first as papillary necrosis with secondary interstitial changes.[16] Interstitial nephritis with Sjogren's syndrome is associated with the sicca syndrome and salivary gland involvement.[17] Although rheumatoid arthritis has been commonly implicated as a cause of interstitial nephritis, rarely if ever, has renal insufficiency resulted without concommitant amyloid deposition, vascular necrosis, analgesic or gold nephropathy.[18] Ruling against these other etiologies in this case include the absence of papillary necrosis, the minimal proteinuria, the lack of electron dense deposits, a normal salivary gland biopsy, and the temporal relationship of complete and rapid return of renal function associated with discontinuing the drug naproxen. This drug can now be added to the ever increasing list of nephrotoxic therapeutic agents.

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Radiology

Case of the Month No. 37

Cary J. Stegman, M.D.
Jonathan M. Levy, M.D.

A 30-year-old white female presents with history of vertex headaches, usually in the morning since the age of 18. These headaches were relieved by aspirin. In the weeks just prior to the CT scan, the patient noted that the headache seemed to be most prominent in the suboccipital area with radiation to the left frontal region. The headaches, however, were still relieved by aspirin. The patient had recently had a single episode of sudden "dropping," associated with light-headedness and weakness of the left lower extremity.

What is your diagnosis?

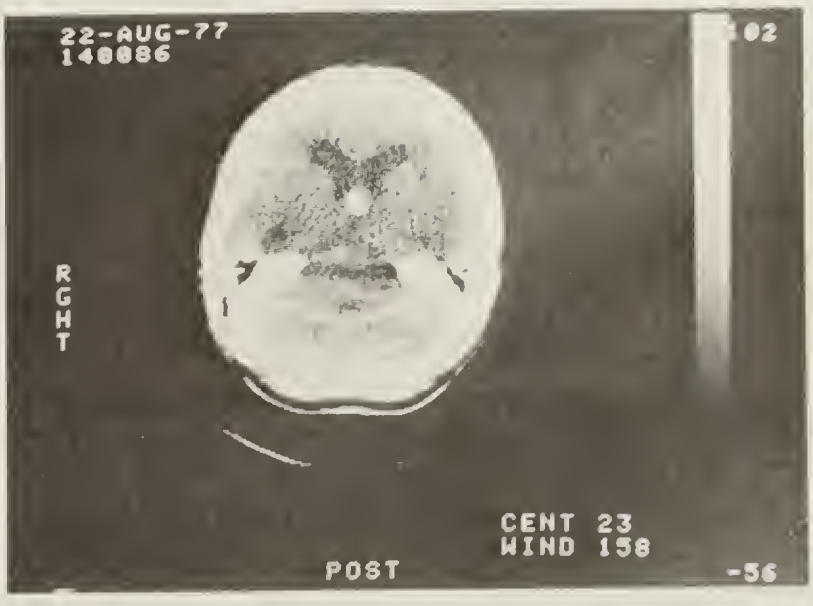

FIGURE 1
NON-CONTRAST CT Scan. What is the abnormality?

From: The Department of Radiology, Scottsdale Memorial Hospital, 7400 E. Osborn Road, Scottsdale, Az. 85251.

Colloid Cyst

ANSWER: COLLOID CYST OF THE THIRD VENTRICLE.

Two findings which should be noted in this case include: 1) Dilated lateral ventricles and 2) a dense spherical mass in the anterior third of the third ventricle, representing the colloid cyst. Pathognomonic of colloid cyst is its greater density than the normal brain on images prior to contrast injection. These findings indicate, with a very high degree of certainty, the diagnosis of colloid cyst.

Colloid cysts arise in neural epithelium located in the tela choroidea of the roof of the third ventricle, at the posterior border of the foramen of Monro. These tumors account for 0.5% of all intracranial tumors and 2% of all gliomas. Having a fibrous epithelial-lined wall, they contain mucoid or dense hyaloid material and usually are 0.3-4.0 cm. in diameter. Symptoms are produced when the cyst becomes large enough to produce obstruction of the foramen of Monro. Although without pathognomonic history or signs, clinical features that would suggest this tumor are a transient, frequently frontal, headache which may be altered by changing posture. The patient may also have brief "drop attacks" characterized by loss of consciousness with flacidity.

The diagnosis of colloid cyst of the third ventricle ha been a very difficult one by clinical and neuroradio graphic methods. In fact, in a series of deaths due t colloid cysts at the Mayo Clinic, 77% were not diagnose ante mortem. Plain radiographic films are not helpful Arteriographic findings are subtle but have been o assistance in making the diagnosis. Prior to CT scanning the most definitive study was either air or positiv contrast ventriculography. These studies do have sever attendant risks. CT, being non-invasive as well as rapidl and easily performed, is the best modality to make thi diagnosis.

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Special Articles

Arizona Perinatal Program —

Past, Present and Future — Part I

Harold D. Gabel, M.D.

Executive Director

The State of Arizona, in 1975, was one of eight regions in the United States to receive a grant from the Robert Wood Johnson Foundation for the development of specialized health care programs to find and care for women with high-risk pregnancies and their infants. The initial five year program, launched with private foundation funds, aims to reduce maternal and infant mortality and morbidity in Arizona through the use of a regionalized approach to health care. This program is the Arizona Perinatal Program, a program of the Arizona Medical Association Foundation, Inc.

Although there had always been a dedicated group of health professionals working tirelessly to improve the conditions for mothers and their offspring in Arizona, their efforts had not succeeded. Arizona had always ranked poorly among the states in the measurements of fetal outcome. In fact, in 1950, Arizona ranked 47th in neonatal mortality among the states.

Let us examine the conditions before the Arizona Perinatal Program and follow through to the present date to see the dramatic accomplishments that have occurred through the use of a regionalization concept. Indeed, things have progressed so dramatically that Arizona ranked second among the states in neonatal mortality recently.

As mentioned previously, although individual efforts have been made by many health care institutions and individuals in Arizona, a collation of effort to improve perinatal outcome, which might be described as a regional system of perinatal health care had not come about. In March of 1964, the Arizona Medical Association's Perinatal and Maternal Mortality Committee brought obstetricians, pediatricians, public health physicians and public health nurses concerned about Arizona's high rates of perinatal and infant death together to discuss the problem.

In 1965, the Committee and the Arizona State Health Department's Bureau of Maternal and Child Health commissioned an epidemiologic study of perinatal mortality for that year. Four conclusions were implicit in that study: (1) principal causes of perinatal morbidity and mortality were related to inaccessibility of high quality maternity care; (2) neonatal mortality is influenced negatively when prompt access to intensive neonatal care is delayed or lacking; (3) the width of geographic distribution of maternal and infant health care must be considered; and (4) reduction of high neonatal and infant mortality rates could be approached most efficiently through a regionalized systems approach.

In 1967, the State Bureau of Maternal and Child Health initiated a study of regionalized care for premature infants and other high-risk neonates. Their hypothesis was that such infants in the hands of specially trained personnel, skilled in the application of the most advanced available techniques in neonatology, would not only improve neonatal survival rate, but also enhance the quality of the neonates life and reduce the numbers of severely damaged newborns requiring prolonged custodial care; and thus, the financial burden for their parents and the State of Arizona would be lessened as well as relieving an enormous burden of human misery for both patients and parents.

Why not a similar and simultaneous program for regionalized perinatal care for high-risk maternity patients? This was the thought brought forth by many perinatal health care providers, but in 1968, manpower and technology for successful obstetrical intervention in high-risk pregnancies were not well developed. There were other organizational and economic reasons peculiar to Arizona but no significant actions were possible until early 1975 when the Arizona Medical Association's Maternal and Child Health Care Perinatal Planning Subcommittee initiated a grant proposal to the Robert Wood Johnson Foundation to support a demonstration of regionalized perinatal care called the Arizona Perinatal Program.

Since its inception, the Arizona Perinatal Program staff has sought to unite and act through health care providers and interested individuals in the provision of the highest quality perinatal health care possible for mothers and babies. It was thought that if maternity patients and their newborns at high-risk were identified early and optimal techniques of obstetrics and pediatrics appropriately applied, a dramatic improvement in the rates of maternal, fetal and neonatal mortality could be produced. A realistic and systematic approach was to be developed so that perinatal health manpower, technology and resources could be applied most effectively and efficiently. This would provide to each patient those resources that were needed, when and where they were needed, in an economically feasible patient oriented manner. The Arizona Perinatal Program, with the help of health care providers and other interested indi-

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From: 810 W. Bethany Home Rd.,
Phoenix, Az. 85014.

viduals, endeavored to create a model for organizing and improving these perinatal resources.

The Arizona Perinatal Program, as an organizing force, would establish a plan and guidelines for a regionalized system of perinatal care but the guidelines were not to be taken as absolutes that must be adhered to and uniformly applied throughout Arizona. It was fully recognized that many localities and areas would not be able to achieve goals that were set immediately. Vast differences among regions in terms of geography, resources, population distribution, etc. suggested that the guidelines promulgated were to be employed with considerable flexibility.

If was fully realized that the practicing physicians of Arizona were the most important component in a regionalized system and only with their cooperation could such a system work. Voluntary participation based on the demonstrated validity of the plan would achieve the end result.

A systemized, cohesive regional network including a number of differentiated resources functioning at various levels of sophistication of care within a region was envisioned. Each component in the system would provide the highest quality of care at an identified level of complexity. The level of function would be based on patient need, location, medical manpower and institutional capability. This system implied the development within a geographic area of a cooperative system of maternal and perinatal health care based upon mutual agreements between hospitals and physicians. All physicians and hospitals in the system of maternal and perinatal health would be linked by a communications network which provides readily available expert telephonic and ambulatory consultation. It would also be necessary to develop basic and continuing education for physicians, nurses and other allied health professionals in the perinatal health care field. Under certain circumstances, efficient and safe transferral of selected maternity cases with complications and selected sick newborns from one hospital to another possessing more comprehensive specialized maternal and perinatal services would be needed.

All components must be organized into a functioning system acceptable to all having as its only objective the improved outcome of all pregnancies. After such a plan is devised, it must be tested.

(*To be continued*)

Out Of Context

Labor Unions, Shop Stewards:

The British Medical Association has been a registered trade union since 1971. Yet for more than a quarter century it has been a defacto trade union, democratically representing doctors at a national level.

In a recent poll 80% of the respondents put central negotiations as a most important function of BMA.

Now a resolution of the Representative Body approved a simple looking motion, "that this meeting supports early appointment of an accredited workplace representative."

These — shop stewards in industrial parlance, "will work in close cooperation with divisional secretaries and hospital representatives caring for the needs of BMA members, as well as recruiting new ones." This is how an editorial in the British Medical Journal in October, 1978 led off describing the new turn in their medical politics.

Some believe it is time for the AMA to also consider the changing times. As it now stands the AMA is the principle "bargaining agent" between members and H.E.W. medical payments, i.e., Medicaid, Medicare and a multitude of separate medical programs such as Crippled Children, Black Lung disease and so forth.

Some of us recall the "extreme anaphyloctoid-like reaction" that many members had to suggestions when the AMA supported a Political Action Fund. Now we are told that such medical PAC's outdo all the unions in the amount of funds raised and spent on political campaigns.

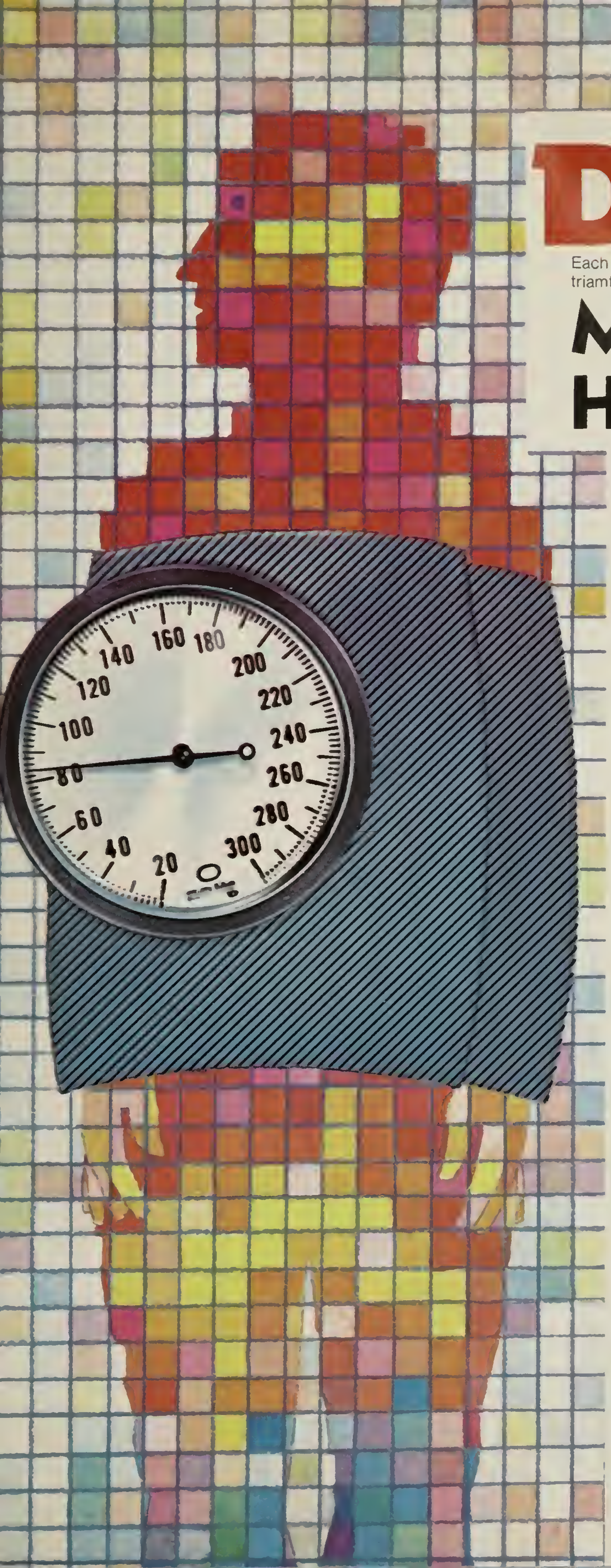
Sure we all lament the British National Health Service and hope for a better system here - but are we not too far down the road politically to stop it?

So Consider —

1. The AMA is now a defacto labor union.
2. Representing the profession on a national level.
3. Tempering or attempting to temper all health legislation.
4. And now we are subjected to regulation by H.E.W. concerning fees, what drugs you shall prescribe, including the generics.
5. The Federal Trade Commission has entered the act stating that advertising is great for the national health.

How long will it be before we need local shop stewards?

John W. Kennedy, M.D.
(Dry Gulch Jake)



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* Warning
This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K+ frequently; both can cause K+ retention and elevated serum K+. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions, nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

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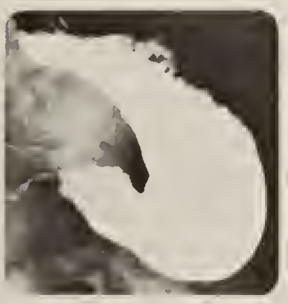
helps control abnormal motor activity with minimal anticholinergic side effects†

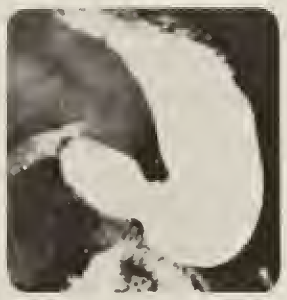
Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating certain functional G I. disorders.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:
King, J.C. and Starkman, N M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964

Merrell

8-3497 (Y515A)

Bentyl®
(dicyclomine hydrochloride USP)

Capsules, Tablets, Syrup, Injection
AVAILABLE ONLY ON PRESCRIPTION.

Brief Summary
INDICATIONS
For use as adjunctive therapy in the treatment of peptic ulcer.
IT SHOULD BE NOTED AT THIS POINT IN TIME THAT THERE IS A LACK OF CONCURRENCE AS TO THE VALUE OF ANTICHOLINERGICS/ANTISPASMODICS IN THE TREATMENT OF GASTRIC ULCER IT HAS NOT BEEN SHOWN CONCLUSIVELY WHETHER ANTICHOLINERGIC/ANTISPASMODIC DRUGS AID IN THE HEALING OF A PEPTIC ULCER, DECREASE THE RATE OF RECURRENCES, OR PREVENT COMPLICATION

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective.

May also be useful in the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis, acute enterocolitis, and functional gastrointestinal disorders); and in neurogenic bowel disturbances (including the splenic flexure syndrome and neurogenic colon).

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis, myasthenia gravis. WARNINGS: In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug PRECAUTIONS Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy Use with caution in patients with autonomic neuropathy; hepatic or renal disease, ulcerative colitis—Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon; hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension, hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

It should be noted that the use of anticholinergic/antispasmodic drugs in the treatment of gastric ulcer may produce a delay in gastric emptying time and may complicate such therapy (antral stasis). Do not rely on the use of the drug in the presence of complication of biliary tract disease Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur ADVERSE REACTIONS: Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention; blurred vision and tachycardia, palpitations; mydriasis; cycloplegia, increased ocular tension; loss of taste; headache; nervousness; drowsiness, weakness; dizziness; insomnia; nausea, vomiting, impotence, suppression of lactation; constipation, bloated feeling, severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. DOSAGE AND ADMINISTRATION. Dosage must be adjusted to individual patient's needs

Usual Dosage Bentyl 10 mg capsule and syrup: *Adults* 1 or 2 capsules or teaspoonfuls syrup three or four times daily *Children* 1 capsule or teaspoonful syrup three or four times daily *Infants.* ½ teaspoonful syrup three or four times daily (May be diluted with equal volume of water) Bentyl 20 mg *Adults* 1 tablet three or four times daily Bentyl Injection *Adults* 2 ml (20 mg) every four to six hours intramuscularly only NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE: The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation Treatment should consist of gastric lavage, emetics, and activated charcoal Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used
Product Information as of October, 1976

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MERRELL NATIONAL LABORATORIES
Division of Richardson-Merrell Inc
Cincinnati, Ohio 45215 U S A

State of the Art

Diabetes and the Kidney

Stanley M. Lee, M.B., F.R.C.P.(C)

The occurrence of diabetes mellitus was recognized almost two thousand years ago when Aretaeus of Cappadocia (A.D.81-138), a Greek physician, described a syndrome of insatiable thirst, polyuria and progressive wasting with a rapidly fatal outcome. Thomas Willis in the 17th Century noted a sweet taste to the urine in these patients — hence the appellation mellitus (mel - honey, Latin), and sugar was confirmed as the major constituent in the urine later in the 18th Century. Early attempts to treat the condition included dietary restriction, but the prognosis remained bleak, and at the turn of the century, the average life span for the juvenile diabetic was 1.2 years, and for the adult onset diabetic - 5 years. Following the introduction of insulin therapy in 1921, the whole spectrum of long term complications of diabetes became apparent, with renal failure contributing a significant role in overall morbidity.

The prevalence of diabetes mellitus in the U.S. is about 1.6%, but a sizeable proportion, perhaps up to 50%, remain undiagnosed. Among the total diabetic population, approximately 100,000 are juvenile onset, insulin dependent. Renal failure is a major cause of death in diabetes. In those individuals developing the disease under the age of 40 years, 35%-40% will die from uremia, and the earlier the onset of the diabetic state, the higher the frequency of renal involvement. Among the total diabetic population, approximately 6% will ultimately require renal replacement therapy.

Diabetes mellitus is now the 5th leading cause of death in the U.S., and costs the national economy 5.5 billion dollars per year. The number of diabetic patients receiving dialysis continues to increase each year, and

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From: University of Arizona, College of Medicine, Department of Internal Medicine, Renal Section, Tucson, Az. 85724.

already contributes in a major way to the total dialysis population.

Diabetes mellitus is unique in its ability to affect several parameters of nephron function (Table 1). The development of renal failure is a consequence of progressive injury involving the glomerulus, tubulo-interstitial structures and the vascular supply. Autonomic neuropathy may lead to neurogenic bladder dysfunction, and iatrogenic nephrotoxic agents may accelerate these changes. These effects will each be considered in turn.

RENAL FUNCTION

In the newly diagnosed insulin-dependent diabetic, significant alterations in renal function are commonly observed. The glomerular filtration rate (GFR) may be elevated as much as 20% above normal. Renal plasma flow (RPF) likewise is increased, but less markedly, resulting in a higher than normal filtration fraction (GFR/RPF). The etiology of these functional alterations remains unknown, but has been variously attributed to increased circulating levels of growth hormone, changes in blood volume and alterations in vascular reactivity involving the afferent and efferent glomerular arterioles. The increased glomerular filtration rate is not generally considered to be a direct consequence of altered glomerular basement membrane permeability. The glomerular filtration rate and renal plasma flow gradually assume a normal range following several weeks of insulin therapy.

Experimentally induced diabetes mellitus in animals is also associated with an elevated glomerular filtration rate. It has been shown that the kidney volume and weight are proportionately increased. Stereologic techniques have demonstrated that although glomerular volume is increased, its cellularity, and that of the tubular structures, is normal. An abnormal water content of the kidney may account for some of these findings. In human diabetes, kidney size tends to remain normal or increased throughout the course of the disease, unless the vascular supply is impaired or pyelonephritic scars supervene.

GLOMERULAR LESIONS

Several lesions may be observed in the glomerulus throughout the course of diabetes (see Table II). Of these, only two are considered typical for diabetes — namely (i) generalized glomerulosclerosis and (ii) nodular glomerulosclerosis (Kimmelstiel-Wilson lesion). The glomerular mesangial area is predominantly involved in both these lesions. The normal masangium consists of cells surrounded by a spongy intercellular matrix. It extends throughout the periphery and central portion of each glomerular lobule, towards the juxtaglomerular apparatus and the vascular pole, where it is in direct contact with the cells of the macula densa. Glomerulosclerosis is apparent as a gradual increase in PAS positive mesangial matrix and occasionally mesangial cells. It may begin as a segmental lesion but eventually progresses to involve the entire glomerulus. The mesangial area gradually becomes sclerotic, and there is compression and obliteration of the glomerular capillary lumina.

TABLE I
ETIOLOGY OF RENAL FAILURE

1. Glomerulopathy
2. Tubulo-interstitial disease
3. Vasculopathy
4. Bladder neuropathy
5. Iatrogenic - toxic

Nodular glomerulosclerosis (Kimmelstiel-Wilson) is considered a pathognomonic feature of diabetes mellitus. Appearing at the periphery of the glomerulus as hyaline masses of PAS positive material, the nodules gradually increase in size and number, encroach upon and obliterate the glomerular capillary lumen. Ultrastructural examination of the nodule suggests that it may originate from the capillary endothelial cell, but its location is predominantly in the mesangium. Despite the fact that it takes 15-20 years for the development of end stage renal failure, a recent study of diabetic patients undergoing renal transplantation showed that early nodular lesions were apparent within 3-4 years in the transplanted kidney.

Exudative lesions, composed of hyaline-like material, are commonly observed on the luminal aspect of the capillary endothelial cell, but are not specific for diabetes. The capsular drop lesion occurs on the inside of Bowmans capsule, between the parietal epithelial cell and its basement membrane, but is also probably not specific for diabetes.

VASCULAR LESIONS

Widespread and accelerated atherosclerosis is common in diabetes, and involves the major renal vessels and large branches. In addition to an ischemic effect on the kidney, atheromatous emboli and associated focal parenchymal infarction may occur. Significant lesions of the major renal arteries may also result in the development of reno-vascular hypertension.

Arteriolosclerosis is also generalized and typically leads to subendothelial hyaline deposits and narrowing of both afferent and efferent glomerular arterioles — the latter considered to be a diagnostic feature of diabetes mellitus. Ischemia involving the region of the renal papilla is probably a contributing factor in the causation of renal papillary necrosis, a not uncommon event in diabetes.

TUBULO-INTERSTITIAL LESIONS

Vacuolization of the tubular cells is frequently observed, and is probably a consequence of prolonged osmotic diuresis related to glycosuria. Hyperlipidemia is associated with lipid accumulation, and the presence of glycogen in tubules (Armanni-Ebstein lesion) was at one time considered to be a pathognomonic feature of diabetic nephropathy. Interstitial nephritis with inflammatory cellular infiltration, fibrosis and scar formation can be observed in those patients having frequent urinary tract infections or chronic pyelonephritis. With long standing diabetes, thickening of the tubular basement membrane is a constant feature. Immunofluorescent examination of

TABLE II
DIABETIC GLOMERULOPATHY

1. Diffuse glomerulosclerosis
2. Nodular glomerulosclerosis (K-W lesion)
3. Exudative lesion
4. Capsular drop lesion

this phenomenon reveals large quantities of albumin and IgG in the tubular basement membrane and the membrane of Bowmans capsule. This is probably a result of a biochemical modification in the membrane composition and/or an alteration in its permeability characteristics, rather than an immunologically mediated phenomenon. It appears to be a specific feature of diabetic nephropathy.

The association of urinary tract infection and diabetes remains a somewhat controversial issue. Acute pyelonephritis is probably not more common in diabetics than in the general population, but asymptomatic bacteriuria appears to occur with a higher frequency. However, in the absence of structural abnormalities, obstruction, or vesico-ureteric reflux, asymptomatic bacteriuria per se does not damage the kidney.

One of the more serious consequences of diabetic nephropathy is renal papillary necrosis. Its exact etiology is unknown, but it probably results from a combination of ischemia and infection, and should be suspected in any diabetic who presents with symptoms of acute pyelonephritis, septicemia, and evidence of ureteral obstruction. Finally, renal carbuncle and xanthogranulomatous pyelonephritis, although rare, should be included as part of the spectrum of diabetic nephropathy.

BASEMENT MEMBRANE LESIONS

Generalized thickening of capillary basement membranes (BM) is a constant feature of diabetes, and has been the subject of considerable controversy. One group has indicated that muscle capillary BM thickening exists in the pre-diabetic state, and is not completely dependent on the duration of diabetes or its therapy. In contrast, the majority viewpoint suggests that progressive BM changes are a consequence of the abnormal metabolic environment characteristic of diabetes. A major problem in answering this issue is the impossibility in achieving euglycemia by pharmacologic means for prolonged periods. Some of the discrepant results among different investigators may be explained by differences in methodology, including tissue preparation and mensuration techniques.

In the kidney, electromicroscopic examination reveals progressive thickening of the glomerular basement membrane (GBM), which is related to the duration of diabetes. The GBM is abnormally permeable to proteins and leads to nephrotic syndrome. There is probably an alteration in the amino acid content of membrane proteins, but again this issue is somewhat controversial.

It is not known whether the alteration in basement membrane thickness is a result of an increased rate of synthesis or a diminished catabolism. It has been postulated that the glomerular mesangium may play a role in the disposition of aging basement membrane. A defect in this aspect of mesangial function could contribute to the BM thickening, and the widening of the mesangial matrix could represent an accumulation of partially degraded basement membrane components.

NEUROPATHY

The development of autonomic neuropathy may have important consequences in the diabetic with impaired renal function. Frequently unrecognized, and usually asymptomatic, neurogenic bladder occurs in greater than 80% of patients with renal failure. Incomplete emptying of the bladder leads to stasis and infection, and a functional obstruction of the urinary tract.

RELATED ENDOCRINE ABNORMALITIES

Insulin requirements will vary in the diabetic with renal insufficiency. Azotemia per se, especially with its associated acidosis, tends to create a state of partial insulin resistance. The kidney, however, possesses insulinase, whose activity decreases as renal failure progresses. In general, less insulin is required as glomerular filtration rate falls, and the patient who starts dialysis or receives a kidney transplant may have a dramatic change in insulin requirements.

Associated with the autonomic neuropathy of diabetes, a decreased activity of the adrenergic nervous system is frequently observed. Postural hypotension and disturbances in gastrointestinal function are common symptoms. In terms of the kidney, there is a diminished activity of renin-angiotensin system, resulting in a syndrome of hyporeninemic hypoaldosteronism. Occurring usually in patients with only a modest decline in renal function (creatinine 2-3 mg/100 ml), these patients have severe, often life-threatening, hyperkalemia and renal tubular acidosis. The renin activity is unresponsive to the usual stimuli of upright posture or volume depletion, but the aldosterone levels rise following angiotensin infusion. This syndrome which also occurs in non-diabetic patients, usually with chronic pyelonephritis, should be suspected when serum potassium levels appear inappropriately elevated for the degree of renal dysfunction. Therapy consists of oral mineralocorticoid replacement on a regular basis.

INTRAVENOUS UROGRAPHY IN DIABETES

Several reports in the past couple of years have demonstrated that contrast media injection, particularly intravenous urography, poses a significant hazard to diabetics with renal insufficiency. Progression to end stage renal failure, or an irreversible decline in glomerular filtration rate, is common. The risk extends to those patients with only minimally decreased renal function (i.e. creatinine 2-3 mg/100ml) as well as those with advanced disease. Hydration status prior to the study does not appear to be helpful in predicting those patients at higher risk. Thus, radiographic studies involving intravenous or intraarterial contrast media should be avoided in all diabetics unless the indications are absolute.

NATURAL HISTORY OF DIABETIC NEPHROPATHY

Normal renal function is well preserved for many years in most diabetics despite the multiple sources of potential injury, and it takes 15-20 years for the development of end stage renal failure. Anecdotal reports and a few controlled studies have suggested that close attention to blood glucose control may decrease the incidence of diabetic nephropathy, or delay its onset, but this issue remains clouded in controversy.

Elevated glomerular filtration rate and renal plasma flow are characteristic features of juvenile onset diabetes in its early stages, but approach the normal range following several weeks of insulin therapy. Low grade proteinuria may be observed after several years of diabetes, but the onset of nephrotic syndrome, often associated with severe hypertension, usually heralds the beginning of a rapid decline in renal function, and the majority of patients will require renal replacement therapy within 3 years.

It is well established that uncontrolled hypertension markedly accelerates diabetic vasculopathy, including nephropathy and retinopathy. The high blood pressure is usually volume dependent with diminished plasma renin activity, but is often very difficult to treat because of the propensity of these patients to develop postural hypotension. An aggressive approach to blood pressure control is mandatory in attempting to slow the progress of renal failure and blindness. Cigarette smoking has been reported to aggravate the course of diabetic retinopathy, and its use should be discouraged in patients with renal insufficiency.

Periodic monitoring for urinary tract infection should be routinely considered, even in asymptomatic patients. Evaluation of bladder function, including residual urine and cystometrograms, is important, especially in those individuals being considered for renal transplantation.

THERAPY

The decision to undertake renal replacement therapy (dialysis or transplantation) should be individualized for each patient. The combination of diabetes and renal failure usually provokes azotemic symptoms at an earlier stage than in non-diabetics, but for optimal results, therapy should be initiated just prior to the onset of symptoms. In most diabetics, a serum creatinine between 5 and 10 mg/100ml should be considered appropriate for starting dialysis or preparing for transplantation.

Early results with hemodialysis in diabetics were very discouraging. The cardiovascular stress occasioned by repeated changes in blood pressure, blood volume and anticoagulation are associated with considerable morbidity and mortality. Myocardial infarctions, cerebrovascular accidents, limb ischemia, and progressive retinopathy are among the commonly encountered problems. Existing and accelerated peripheral vascular disease adds to the difficulties in maintaining adequate sites for vascular access which are highly susceptible to infection.

The survival results of patients undergoing cadaveric renal transplantation are almost identical to those of hemodialysis and show a 30% mortality in the first year. By three years, almost 70% of patients have died.

Transplantation from a living related donor is currently the optimal mode of therapy, with patient survival approaching 80% for the first year. Unfortunately, the occurrence of diabetes in related family members often precludes related donor kidney transplantation. Pretreatment of cadaveric donors with high dose immunosuppression prior to nephrectomy is a promising alternative, and in one study gave survival statistics approaching those for living related donors.

Renal replacement therapy, including dialysis and transplantation, although capable of prolonging the life of patients with end stage diabetic nephropathy, is, at best, a limited compromise. As with most situations in medicine, prevention is the ideal therapy. The introduction of insulin over 50 years ago created the opportunity to observe the natural history of diabetic nephropathy, but our understanding of its pathogenesis remains incomplete. Animal experiments have demonstrated that pancreatic islet cell transplantation can reverse the changes of early diabetic nephropathy and it is probable that endocrine factors apart from insulin may play a significant role in modulating the metabolic environment of the diabetic. Improved methods for automated insulin administration, the development of new hypoglycemic pharmacologic agents and a broader understanding of the pathophysiology of diabetic vasculopathy may soon provide a means to prevent and reverse the natural history of this disease.

REFERENCES

References available on request.

ACKNOWLEDGMENTS

The author wishes to express appreciation to Frances Campion for secretarial assistance.

This work was supported in part by a National Institutes of Health Biomedical Research Support Grant.

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The Arizona Rural Underserved Incentive Program

The University of Arizona College of Medicine has taken a four-pronged approach to increasing the number of physicians serving in rural underserved areas of Arizona. First, the College of Medicine has committed itself to provide information to young people from these areas on the educational opportunities available in health care, particularly medicine. Secondly, the Admissions Committee of the College of Medicine has taken an affirmative action approach to rural applicants, i.e., individuals who have spent more than half their lives in rural Arizona and who desire to practice in such an area. Thirdly, opportunities are provided to medical students with these interests to gain experience through clerkships in rural and underserved areas. Finally, the University of Arizona, in cooperation with the state legislature, has initiated the introduction of a rural underserved incentive program.

In August 1977 a new program was developed which is known as the Medical Student Loan Program. No funds were provided by the legislature until August 1978. This program is designed to provide financial support through loans for ten students per year. These students must be enrolled in the University of Arizona College of Medicine and must have a desire to provide primary care in a rural underserved area in the state of Arizona. Each year the Medical Student Loan Board, composed of seven members, three of whom are appointed by the Governor, two by the Arizona Board of Medical Examiners, one by the President of the University of Arizona, and the Director of the Department of Health Services or his or her designate, meet and select recipients for this program. The accepted applicants sign a contract to provide one year of medical service in a designated rural underserved area for each year of this loan. A minimum of two years of service is required. After medical school gradu tion the recipient must begin service afte minimum of one year or a maximum three years of residency. For each year medical service provided a year of lo and interest will be deemed forgiven paid.

Rural underserved areas are designat by the Department of Health Services. the present time this Department is maki every effort to include as underserv areas the designated sites which have al been approved by the National Heal Service Corps. In this way it will possible for recipients of this loan to jo the National Health Service Corps at t completion of their medical education a residency program and serve at develop sites while receiving a fixed salary. It is t hope that these recipients will not only this type of service in order to pay the loan obligations, but will continue practice medicine in these or simil locations. Once this program is function it should provide an average of t physicians per year for underserved cor munities.

During the time the loan recipients a students at the University of Arizo College of Medicine opportunities will made available to them to participate medical experiences in areas similar those which will ultimately be practi sites. At the present time the College Medicine has developed preceptorship a rangements in communities which are ve similar to communities which have pr viously been considered underserved. T student recipients also will be required renew their contracts each year an thereby re-establish their commitment this particular program.

Under this program it is possible for a individual whose goal is to serve in a rur underserved area of Arizona to receive h or her medical education at virtually n cost in return for four years of medic service in such an area. Programs simil to this have been effective in providi physicians for rural underserved areas i such states as New Mexico, Kentuck Mississippi and Illinois. Arizona loo forward to success exceeding that of the states.

Andrew Goldner, Ph.D.
Associate Dean for Student Affairs
College of Medicine
University of Arizona

Louis J. Kettel, M.D.
Dean, College of Medicine
University of Arizona

Auxiliary Highlights

FACETS is the name chosen for the official Auxiliary publication sent by National directly to each Auxiliary member. The popular magazine format far exceeds its predecessors' appeal. In fact, history reveals roots set in pretty dry ground if National communication is traced back even to the old Bulletin of 1940 through 1965. Sales contests were required to promote delivery of the booklet, but even a rudimentary glance was probably the exception for any Auxilian not duty driven to refer to the serious handbook, the truth be known and all due respect to the dignified effort.

An inventive shake-up occured in more recent years when a non-auxiliary agency began circulating a colorful, slick papered magazine aimed specifically toward doctors' wives. Commercial exploitation became a consideration plus the obvious concern of enticement to read a publication easily more attractive than the staid National publications.

Auxiliary rallied with modifications designed to create greater readability and appeal of its own, but efforts were doomed in competition as the renegade free mailer featured stories and pictures of doctors' wives engaged in interesting activities throughout the country. The hobbies and creative passtimes depicted somehow translated to Auxiliary program without portfolio, and non-control and possible misrepresentation posed potential problems.

Omitting description of the resulting heads together exchange of concerns over the shadowing publication, it suffices to say that Auxiliary effectiveness in facing problematic circumstances was tested and found to be adequate as noted by Auxiliary's 1975 copyright date.

Now, the four times per year publication carries colorfully illustrated features involving not only Auxiliary program emphasis, but doctors' concerns as well. Contents include Issues, Events, and People; Focus on Auxiliary program; Legislative Update; and a full range of timely topics relating to the likes of public relations, successful marriages, financial skills, time management, estate planning, volunteerism, window washing, and a whole lot more.

Being official and still appealing would surely become a challenge to any organization's editorial staff, but the many faceted FACETS serves up a palatable array of valuable subjects to the receptive Auxiliary member today.

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ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

PURCHASING COMMITTEE — WESTERN PHYSICIANS PURCHASING ASSOCIATION

The organizational meeting of the Purchasing Committee — Western Physicians Purchasing Association of the Arizona Medical Association, Inc., held at 810 West Bethany Home Road, Phoenix, Arizona, on Friday, December 8, 1978, a quorum being present, convened at 6:41 p.m., John F. Kahle, M.D., Chairman, presiding.

THE WESTERN PHYSICIANS PURCHASING ASSOCIATION — ITS HISTORY & DEVELOPMENT

In an effort to fully inform the committee as to the formation of the Western Physicians Purchasing Association, Bruce Robinson, Executive Director of the Arizona Medical Association, Dr. Kahle, Chairman of this committee and President of the WPPA, and Mr. Allen, Executive Director of the WPPA, each addressed the members regarding initial discussions among the several state associations and the research which ultimately developed the new purchasing association, the initial negotiations with suppliers, the establishment of the main office in Cheyenne, Wyoming, and the basic program and how it was presently set up to provide the most prompt and efficient service to participating physicians.

THE SCHERER CORPORATION CONTRACTS

Price Evaluation and Suggested Additions

Mr. Allen presented to the committee for its review and discussion a catalogue prepared by Scherer containing a breakdown of the items thus far being supplied and pricing for such items. The committee discussed at length not only those items which were included in the document but additional items which might or should be added, at which point it was agreed that members of the committee would prepare their suggested additions in writing and submit them to Mr. Allen who would, in turn, negotiate to have the same included either by Scherer or other suppliers.

DRUGS TO BE OFFERED BY WPPA

Following a lengthy discussion as to drugs normally used by physicians' offices and the necessity of offering these and other drugs to the membership, it was agreed that Mr. Allen would be provided lists of drugs by name, with specificity as to manufacturers' names, so that suppliers could be contacted and products secured for inclusion in the catalogue at the earliest possible date.

REPORT ON OTHER CONTRACTS AND PLANS

Mr. Allen reported that several suppliers had been contacted regarding possible additions to the existing products and he was awaiting further discussions with them. He advised that the immediate plan was that the catalogue furnished to participating members would be in the form of a 3-ring binder so that supplements could easily be added or products deleted at any time with a minimum of effort.

OTHER BUSINESS

Membership

Following a discussion regarding some of the problems which had arisen since the initial mailing to ArMA members of the WPPA brochures, it was agreed that a second mailing of these brochures should incorporate several of the items from the catalogue, indicating prices, etc., for comparison evaluation by the physicians and their staff.

FINANCE COMMITTEE

The meeting of the Finance Committee of the Arizona Medical Association, held at 810 W. Bethany Home Road, Phoenix, Arizona, on Saturday, December 9, 1978, convened at 9:10 a.m., Neopito L. Robles, M.D., Treasurer and Chairman, presiding.

PIMA COUNCIL TO IMMUNIZE ARIZONA'S CHILDREN

The committee considered the request for funds of the Pima Council to Immunize Arizona's Children dated October 26, 1978, in conjunction with the recommendation of the Professional Committee and the endorsement of the Executive Committee. While the committee was in agreement that the concept of the program was one which deserved great support from the Association, it was determined that the 1978 budget did not contain funds with which financial support could be given at this time and

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT, WHILE THERE ARE PRESENTLY NO FUNDS AVAILABLE FOR SUCH PURPOSE, THE REQUEST OF THE PIMA COUNCIL TO IMMUNIZE ARIZONA'S CHILDREN BE HELD IN ABEYANCE, TO BE RECONSIDERED AT A TIME WHEN THE BUDGET WOULD ALLOW FOR ADDITIONAL CONTRIBUTIONS TO DESERVING AND WORTHWHILE PROJECTS.

EMPLOYMENT OF RESEARCH ANALYST

The committee considered and discussed at length the recommendation of the Governmental Services Committee regarding the need to employ a research analyst to keep all committees and the Association as a whole fully abreast of all state, county and federal activities affecting the medical profession. While it was determined that such research analyst would certainly be most beneficial, no action was taken at this time, pending further investigation into the possibility of the county medical societies sharing in the use of and payment for such an employee.

PREPARATION OF 1980 BUDGET

Bruce Robinson briefly described to the committee the format followed in past years regarding preparation of the annual budget and advised that, since it was time to begin preparation of the 1980 budget, he would like input from the committee members as to what changes, if any, they would like insofar as the committee's participation in or review of such budget prior to finalization. Following a thorough discussion of the matter, it was determined that Mr. Robinson and staff members would prepare the budget figures for 1980 as they had in past years for submission to the Chairman for his review; however, in conjunction therewith

IT WAS MOVED AND CARRIED THAT THE BUDGETS FOR ALL ASSOCIATION COMMITTEES FOR 1980 WOULD BE ESTABLISHED AT AN AMOUNT EQUAL TO 10% LESS THAN THE AMOUNT ALLOCATED FOR SUCH COMMITTEE IN 1978.

SCIENTIFIC ASSEMBLY COMMITTEE

The meeting of the Scientific Assembly Committee of the Arizona Medical Association, Inc., held at 810 W. Bethany Home Road, Phoenix, Arizona, on Saturday, December 9, 1978, a quorum being present, convened at 1:26 p.m., Marvin C. Schneider, Chairman, presiding.

1980 MEETING — SPECIALTY SOCIETY INVOLVEMENT

Dr. Hurley, as Chairman for the 1980 Annual Meeting, addressed the specialty societies present, advising that the 1980 Annual Meeting was scheduled to be held April 30-May 4, 1980 at the Registry Resort in Scottsdale, that the University of Colorado had confirmed that it would provide the core faculty for such meeting, and that the Association was desirous of having specialty societies become more involved throughout the meeting by possibly holding their own individual meetings as a portion thereof, by requesting specific University of Colorado faculty to provide programs with their specialty in mind, or by requesting the Association to approach others more qualified in a certain field of expertise to present a portion of the 1980 meeting.

Dr. Hurley then requested that each representative report back to his or her designated specialty society the desire of the Association to receive from each specialty society a written statement as to how they would like to participate in the 1980 meeting, together with any requests they might have as to speakers or programs which might bring greater response from the physicians in their specialty field. Since few plans have been finalized and the meeting is still in the developmental stages, it was the consensus of opinion that all requests received within the near future would be able to be considered and included in an effort to make the 1980 meeting one of high attendance as well as an educational experience in every field of medicine.

LOCAL PAPER SELECTION

IT WAS MOVED AND CARRIED TO ACCEPT THE FOLLOWING PAPERS SUBMITTED BY ARIZONA PHYSICIANS:

1. Pedophilia (Child Molesting): Differential Diagnosis, Identification and Treatments — Willard S. Gold, M.D.
2. Urticaria — Etiology, Pathogenesis and Treatment — Bryan R. Updegraff, M.D.
3. Pituatary Tumors: Recent Diagnostic and Therapeutic Advances — Marshall B. Block, M.D., William H. White, M.D., and Jeffrey Black, M.D.
4. Fibrinolytic Activator and Inhibitor Activity in Malignant Neoplasms — Alfred S. Gervin, M.D., James D. Malone, M.D., and Wesley Moore, M.D.
5. A New Application of EKG Treadmill Testing: The Elderly For Exercise Prescription, with Follow-up Test Results — Julius Schwimmer, M.D., F.A.C.C.
6. Legionnaire's Disease — Update — Karen M. Starko, M.D.

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INDICATIONS: *Therapeutically*, (as an adjunct to systemic therapy when indicated), for topical infections, primary or secondary, due to susceptible organisms, as in: infected burns, skin grafts, surgical incisions, otitis externa; primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia); secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis); traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components. Do not use in the eyes or in the external ear canal if the eardrum is perforated.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.

7. Presurgical Evaluation of Patients with Recurrent Pancreatitis: Emphasis on the Value of ERCP — George E. Burdick, M.D.
8. Long-Term Intermittant Oxygen Therapy — A New Method — W. Sam Williams, M.D., F.A.C.P.

SCIENTIFIC EXHIBITS

IT WAS MOVED AND CARRIED TO ACCEPT THE FOLLOWING SCIENTIFIC EXHIBITS:

1. Arthroscopic Knee Surgery — Eugene J. Chandler, M.D.
2. 55° Oblique Hilar Tomography — J.M. Levy, M.D., C.J. Stegman, M.D., P.W. Nykamp, M.D., J.K. Crowe, M.D., and M.S. Levy, M.D.
3. The Transsphenoidal Approach to the Sella Turcica — Lewis J. Brown, M.D.
4. The Collaborative Teaching of Human Sexualty — Jackson A. Smith, M.D., and Domeena C. Renshaw, M.D.
5. Non-Invasive Peripheral Vascular Laboratory Examinations of Carotid Artery Occlusive Disease — John M. Johnson, M.D., John Quatromoni, M.D., Sandra Morgan, R.T., and Jo Ann Riley, R.T.
6. Modern Treatment of Chronic Pain — Robert H. Barnes, M.D., and Robert B. Posner, M.D.
7. Vascular Ring — Ravi Koopot, M.D., Edward B. Diethrich, M.D., and Robert L. Williams, M.D.
8. Coccidioides Immitis — Thoracic Roentgen Manifestations and Complications — Glenn C. Cook, M.D., John C. Bjelland, M.D., and Irwin M. Freundlich, M.D.
9. Rib Changes in Generalized Disease — Alex Newman, M.D., and Denise M. Mulvihill, M.D.
10. Early Rehabilitation & Shortened Hospitalization by Use of Rigid Internal and External Fixation of Fractures — Saul N. Schreiber, M.D.
11. Sleep Aprea Syndrome: A Common Clinical Problem — Richard M. Riedy, M.D., and Bernard Levine, M.D.
12. Brainstem Auditory Evoked Response Assessment — Sandra T. Hirshburg, MMS, CCC-A, and Robert J. Trzepkowski, M.A.

IT WAS MOVED AND CARRIED THAT IN THE FUTURE, WHEN SOLICITING SCIENTIFIC PAPERS AND EXHIBITS, REQUEST BE MADE OF APPLICANTS SUBMITTING ONE OF EACH TO INDICATE THEIR PREFERENCE AS TO WHICH, IN THEIR OPINION, WOULD BE THE BETTER PRESENTATION.

AUXILIARY PROGRAM

Eloise Clymer advised the committee that the joint program of the Association and the ArMA Auxiliary scheduled to be held Thursday, April 26, 1979 beginning at 8:00 a.m., was being finanized, with the only unresolved matter being a topic for the presentation. Following a discussion by the committee it was agreed that the title "Physicians' Family Circus" be used if the Auxiliary was able to obtain the agreement of Bil Keene of the Arizona Republic to furnish some of the art work for posters, etc. In the event Mr. Keene was unable to do so, it was agreed that the title "Physicians' Families" could be used at the sole discretion of the Auxiliary.

Mrs. Parsons requested that the program of Dr. Thomas E. Bittker, because of spouse participation and a conflicting Auxiliary meeting, be moved back one-half hour on Friday, April 27, 1978, from 2:00 to 2:30 p.m. The consensus of opinion was that this would be no problem and that Dr. Bittker would be so informed.

PHILLIP S. HENCH LECTURESHIP

The committee reviewed the offer of Sanford H. Roth, M.D., dated October 19, 1978 and discussed the offer for Dr. Randolph C. Blodgett to participate in the 1979 Annual Meeting of the Association.

IT WAS MOVED AND CARRIED THAT DR. RANDOLPH C. BLODGETT BE REQUESTED TO PRESENT A HALF HOUR PROGRAM ON FRIDAY, APRIL 27, 1979, FROM 2:00 to 2:30 P.M.

HEALTH EVALUATION AND LONGEVITY PLANNING FOUNDATION

The committee reviewed the offer of the H.E.L.P. Foundation dated September 14, 1978 to participate in the 1979 Annual Meeting and following a discussion of the matter,

IT WAS MOVED AND CARRIED THAT THE PROPOSAL OF THE H.E.L.P. FOUNDATION FOR PARTICIPATION IN THE 1979 ANNUAL MEETING OF THE ASSOCIATION BE REJECTED.

OTHER BUSINESS

University of Arizona

U of A letter dated September 15, 1978 offering to do 1981 meeting. RECEIVED.

Confirmation from AMA

AMA letter of November 15, 1978 advising that President Tom E. Nesbitt, M.D., will attend the 1979 Annual Meeting. RECEIVED.

University of Colorado

Letter from the University of Colorado confirming that they will provide the core faculty for the 1980 Annual Meeting dated September 5, 1978. RECEIVED.

Board of Directors' Actions

Letter dated September 25, 1978 confirming appointment by the Board of Directors of James M. Hurley, M.D., as Vice Chairman of the Scientific Assembly Committee for 1978-79 and Chairman for 1979-80. RECEIVED.

Letter dated September 25, 1978 confirming committee's action that the 1981 meeting be held in the Phoenix-Scottsdale area. RECEIVED.

1. **The Pointe** —Confirmation for 1981 Meeting.

IT WAS MOVED AND CARRIED THAT THE POINTE BE CHOSEN AS THE LOCATION FOR THE 1981 ANNUAL MEETING OF THE ASSOCIATION.

LEGISLATIVE COMMITTEE

The meeting of the Legislative Committee of the Arizona Medical Association, Inc. held Wednesday, December 13, 1978, at 810 W. Bethany Home Road, Phoenix, Arizona, convened at 7:29 p.m., Selma E. Targovnik, M.D., Chairperson, presiding.

DEFINITION OF TERMS

Dr. Targovnik explained that the following definition of terms will be used in explaining the Association's legislative activities:

ACTIVE SUPPORT: Means approval of bill and maximum staff time and financial expenditure (including legal counsel) will be made to achieve enactment.

GENERAL SUPPORT: Means approval of the principle of the bill, but that staff time and financial expenditures will be limited.

NO ACTION: Means no position has been taken one way or another on the bill.

NON-SUPPORT: Means disapproval of the bill, but that staff time and financial expenditures will be limited to defeat the bill.

ACTIVE NON-SUPPORT: Means disapproval of bill and that maximum staff time and financial expenditure (including legal counsel) will be expended to achieve defeat of the bill.

ACTIVE STUDY: Means the bill contains both supportable and opposable elements.

LEGISLATIVE REVIEW

FINAL STATUS REPORT

The Final Status Report of the Last Legislative Session was received by the Committee for information only.

NURSES PRACTICE ACT (NURSE PRACTITIONERS)

Senator Lindeman addressed the Committee explaining that it was her intention to create a new advisory committee to the Board of Nursing to approve rules and regulations for the Nurse Practitioner. This advisory committee would take the place of the Joint Board of Medical and Osteopathic Examiners as it pertains to nurse practitioners. An initial draft of her thoughts was discussed. It was pointed out that the House of Delegates, in 1977, had adopted a resolution providing "that physician extenders be under the control of the Joint Board of Medical and Osteopathic Examiners to provide adequate educational training and certification mechanisms for all physician extenders as well as assuring that these physician extenders have adequate physician supervision."

IT WAS MOVED AND CARRIED TO TAKE NO ACTION AT THIS TIME ON LEGISLATION PROVIDING FOR A REVISION OF THE NURSE PRACTICE ACT AS IT PERTAINS TO NURSE PRACTITIONERS.

ARIZONA IMMUNIZATION LAW

Ms. Ruth Ogden informed the Committee that the Pima Council to Immunize Arizona's Children, a coalition of interested health professionals and volunteers, was formed in response to HEW's national Immunization Initiative. The goal of the Initiative is to raise immunization levels among the nation's children to 90% by October of 1979.

The Council has developed a statewide program to increase awareness of the need for early childhood immunizations against polio, measles, mumps, rubella, diphtheria, tetanus and pertussis. Currently the Council is introducing a parent-maintained immunization record designed specifically for Arizona as a focal point of the campaign. However, it is the Council's conviction that the most effective way to raise Arizona's immunization levels is to strengthen the existing school immunization law, which at present is not comprehensive in scope.

The present law requires immunization only for kindergarten children and transfer students through grade 8 in the public schools. Preschool children are particularly susceptible to these serious diseases, and in addition Arizona is experiencing a growing number of measles and rubella epidemics among teenagers; neither of these age groups is affected by the existing law. Students in private and parochial schools are currently outside the scope of the law. The present law allows a child's immunization record to be based only on parental recall which is often inaccurate.

It is the intent of the proposed revision of the law to extend protection against these vaccine-preventible diseases to all Arizona children by including all ages of children in all schools through grade 12 and by requiring adequate proof of immunization to insure that children are in fact immunized against specific diseases, and to insure that unprotected children can be identified and immunized. (Copy of the proposed legislation is on file.)

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT THE INTRODUCTION AND PASSAGE OF THE PROPOSED MODIFICATIONS TO THE IMMUNIZATION ACT.

MEDICAL PRACTICE ACT - ADVERTISING

Mr. Jacobson explained that last year we were unsuccessful in amending the Medical Practice Act as it pertains to advertising in accordance with the Supreme Court's decision. We are, therefore, wishing to re-introduce the legislation to conform.

IT WAS MOVED AND CARRIED TO INTRODUCE AND ACTIVELY SUPPORT LEGISLATION DEFINING UNPROFESSIONAL CONDUCT IN THE PRACTICE OF MEDICINE WITH RESPECT TO ADVERTISING.

MEDICAL PRACTICE ACT - CME

Mr. Boykin presented the proposal by the Board of Medical Examiners clarifying the Act as it pertains to Continuing Medical Education requirements. It was pointed out that the current language was restrictive and difficult to implement. Broad authority to be implemented through rules and regulations is desirable.

IT WAS MOVED AND CARRIED TO GENERALLY SUPPORT THE CONCEPT OF PROVIDING BROAD AUTHORITY TO THE BOARD OF MEDICAL EXAMINERS REGARDING CONTINUAL MEDICAL EDUCATION.

PHYSICIANS' ASSISTANTS - COMPENSATION

Mr. Boykin explained that the Physicians Assistants Act as was adopted two years ago, did not include the provision for compensation for personnel or Board members as generally provided by law. Also, legislation did not provide that the Board may keep its licensure fees as other 90-10 agencies are allowed. The Joint Board of Medical and Osteopathic Examiners request the Association's assistance in correcting these omissions.

IT WAS MOVED AND CARRIED TO GENERALLY SUPPORT LEGISLATION PROVIDING FOR COMPENSATION TO EMPLOYES AND BOARD MEMBERS AND FOR THE JOINT BOARD OF MEDICAL AND OSTEOPATHIC EXAMINERS FUND.

CERTIFICATE OF NEED - ARIZONA HOSPITAL ASSOCIATION

Mr. Chic Older presented proposed legislation which would provide for:

1. Attempt to clarify the definition of health related services as pertains to the CON process.
2. Changing expenditure threshold amount from $100,000 or 3% of budgeted annual expenses (whichever is less) to $150,000 or 7% of budgeted expenses (whichever is less).
3. Redefining new medical services in an effort to eliminate some of the unnecessary CON hearing caused by literal interpretation of this language.
4. Change present $50,000 total threshold for substantial changes in medical services to $150,000.
5. Introduction of language allowing clinical department interchangeability of beds if change will result in increased expenditures of no more than $150,000 within 12 months.
6. Eliminate the "catch 22" clause requiring proof that applicant conforms to the health plan adopted by the HSA.
7. Addition of due process mechanisms in the designation of CON committees.

IT WAS MOVED AND CARRIED TO PROVIDE GENERAL SUPPORT TO PROPOSED AMENDMENTS TO THE CERTIFICATE OF NEED LAW BY THE ARIZONA HOSPITAL ASSOCIATION.

STATE CONFORMANCE to 93-641

Dr. Dandoy informed the Committee that in order to satisfy Title XV and XVI of the federal Public Health Service Act, P. L. 93-641, as implemented by federal regulations, 42 C. FR. 4001 and 18605, the following state statutory amendments are necessary:

1. Present law requires that recommendations from Health Systems Agencies to the State Health Planning and Development Agency must be followed unless they are arbitrary, capricious or not based upon substantial evidence. Under the Federal Act, the State Health Planning and Development Agency must be free to accept or reject recommendations from the Health Systems Agencies without limitations.
2. The Federal Act requires that all Health Maintenance Organizations first obtain a Certificate of Need before offering health services whereas some are exempted under our present statute.
3. Arizona law does not require a Certificate of Need for bed redistribution or relocation whereas the Federal Act requires one where 10 or more beds or 10% of the facility's capacity over two years is affected.
4. The Federal Act requires a Certificate of Need for all new health services regardless of capital expense, while under Arizona law it is only required if the capital expense exceeds $100,000.
5. A Certificate of Need decision must be appealable by the "affected public" in addition to the applicant or the Health Systems Agency as presently provided under our law.

The above proposed amendments are not all inclusive as other procedural changes will also be requested.

Considerable discussion ensued.

IT WAS MOVED AND CARRIED TO TAKE NO ACTION ON LEGISLATION PROVIDING FOR CONFORMANCE TO PUBLIC LAW 93-641 AT THIS TIME.

MENTAL COMMITMENT ACT

Drs. Campbell and Dandoy explained that the 1974 Arizona Legislature extensively revised Arizona's Civil Commitment Law (A.R.S. 36-501 ff) to bring it into conformity with court decisions, professional recommendations, and recommendations emerging from a 1979 University of Arizona - College of Law study of commitment practices in Arizona.

Concerns have been voiced by both professional and law enforcement personnel regarding the law's unnecessary restrictiveness which often interferes with patient care and its procedural complications which occasionally make it difficult to obtain hospitalization for mentally ill persons in acute distress.

A bill is being prepared which will provide:

1. Changes in the definitions of danger to others and danger to self which clarify the extent to which threats may be taken into consideration in filing petitions for court-ordered evaluation. These revised definitions will facilitate the admission of potentially dangerous mentally ill persons without allowing widespread abuse of the commitment process.
2. Revisions in the process of emergency detention which will facilitate bringing mentally ill persons who are imminently dangerous to an evaluation agency for emergency examination. Presently, there is no mechanism for accomplishing this and this is of serious concern to law enforcement agencies as well as mental health professionals.
3. Clarification of the definitions and procedures relative to the handling of persons who are gravely disabled as a result of a mental disorder. This is a high priority since confusion exists within the mental health community and the courts regarding this part of the law. These revisions will clarify when the commitment law, in contrast to the probate code should be utilized.
4. Clarification of the role of county attorneys in the commitment process.
5. Clarification of the concept of less restrictive alternatives for court-ordered treatment.
6. Technical amendments which will revise the language of the law and make it internally consistent.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT AMENDMENTS TO THE MENTAL COMMITMENT ACT.

SUPERINTENDENT OF STATE HOSPITAL

Dr. Dandoy explained that this bill would delete from state law the specific powers and duties of the Superintendent of the State Hospital but would retain the statutory qualifications for that position. The reason for this proposal is that existing law does not reflect the organization of the Department of Health Services as provided by the reorganization law of 1973. Specifically, that law requires the Director to structure the Department in a certain manner and also allowing for the deputization of personnel to perform any and all duties of that office. In view of that legislative mandate, it does not appear appropriate for a position within the Department to have distinct statutory duties and functions which may conflict with the responsibility and authority of the Director. Rather, the duties of that position should be consistent with the total organization of the Department as specified by the Director.

Dr. Campbell expressed some concerns with this legislation in behalf of the Psychiatric Society.

IT WAS MOVED AND CARRIED THAT NO ACTION BE TAKEN ON LEGISLATION PROVIDING FOR THE DELETION FROM STATE LAW OF THE SPECIFIC POWERS AND DUTIES OF THE SUPERINTENDENT OF THE STATE HOSPITAL.

ZONING FOR COMMUNITY RESIDENTS

Dr. Dandoy identified the need for changes in the present zoning ordinances which are discriminating against the needs of the mentally ill. The Department of Health Services will be proposing legislation in regard to zoning guidelines.

IT WAS MOVED AND CARRIED TO TAKE NO ACTION ON LEGISLATION PROVIDING FOR CHANGES IN ZONING ORDINANCES WITH REGARD TO THE MENTALLY ILL.

FUNDS FOR PATIENT BENEFIT PURPOSES.

Dr. Dandoy explained that there is a lack of funds available to residents of Halfway Houses to assist them with fiscal support which allows them to pay for personal items, transportation to and from job interviews and volunteer program settings to which they are assigned, and for minimal personal clothing that will allow them to make a good impression in job interview and volunteer program settings. Statutory revision would allow the Southern Arizona Mental Health Center to utilize some of its resources to generate a limited amount of funds which could be used for Halfway House patients to solve the above problems.

IT WAS MOVED AND CARRIED TO TAKE NO ACTION ON LEGISLATION PROVIDING FOR FUNDS FOR PATIENT BENEFIT PURPOSES.

CHILD DAY CARE LICENSURE AMENDMENTS

Dr. Dandoy explained the need to amend the Child Day Care Licensure Law with reference to the exemption section, eliminating the statutory mandate to visit all facilities two times annually, and to change the licensing period from one year to three years.

IT WAS MOVED AND CARRIED TO TAKE NO ACTION ON LEGISLATION PROVIDING FOR AMENDMENTS TO THE CHILD DAY CARE LICENSURE LAW AS PROPOSED BY THE DEPARTMENT OF HEALTH SERVICES.

HOME HEALTH SERVICES AMENDMENTS

Dr. Dandoy, on behalf of the Department of Health Services, explained to the Committee that amendments are being prepared to provide for home health services benefits in insurance contracts as an alternative to institutional care.

IT WAS MOVED AND CARRIED TO OFFER GENERAL SUPPORT TO PROPOSED LEGISLATION PROVIDING FOR HOME HEALTH SERVICES.

BLOOD TESTS FOR PREGNANT WOMEN

Dr. Dandoy discussed the Department of Health Services' proposed amendment to ARS §36-693 which will require attending physicians to take or cause to be taken a blood sample of pregnant women and submit it for a standard Serology Test for Syphilis during the final three months of pregnancy as well as during the first three months of pregnancy which should eliminate the possibility of congenital syphilis.

IT WAS MOVED AND CARRIED TO OFFER GENERAL SUPPORT TO THE PROPOSED LEGISLATION PROVIDING FOR BLOOD TESTS FOR PREGNANT WOMEN DURING THE FINAL THREE MONTHS OF PREGNANCY.

VITAL RECORDS

Dr. Dandoy explained to the Committee the need for the below recommended changes based on the Model State Vital Statistics Act — 1977 Revision as proposed by the National Center for Health Statistics, Department of Health, Education and Welfare; the model act has been approved by the Committee on Suggested State Legislation of the Council of State Governments. The main objectives of the Department in adopting portions of the 1977 Revision are: (1) to provide improved birth and death registration procedures for general public; (2) to insure the vital records needs of the public are being met; (3) to incorporate current social customs and practices and current technology into the policies and procedures for the vital statistics system; and (4) to promote the uniformity of these policies and procedures to the end that all vital records will be readily acceptable in all places as prima facie evidence of the facts therein recorded.

Recommended changes are:

Sections 36-322 and 36-327. Birth and Death Registration. Amended to provide for the registration of births and deaths for those births or deaths occurring on a moving conveyance while in international waters or air space or a foreign country or its air space and the child or body is first removed from the conveyance in this state.

Section 36-322C. Birth Registration. Amended to provide for the certification of a birth certificate by the person in charge of the institution if the physician, or other person in attendance, is not available to certify the facts of birth within the prescribed time period.

Section 36-324.01. Judicial procedure to establish facts of birth. Added to provide for an alternative procedure for the delayed birth registration for those individuals not qualifying under Section 36-324. If a delayed birth certificate is rejected under Section 36-324, an individual cannot — under present law — document his/her birth as having occurred in Arizona.

Section 36-329. Fetal death registration. Amended to provide for fetal death registration when the gestation period is unknown. "A weight of 350 grams or more" is added.

Section 36-331. Reports of death; disposal-transit permits; disinterment permits. Amended to delete reference to coroner investigation and formal funeral rites.

Amended to indicate a disposal-transit permit shall not be required for fetal deaths of less than twenty weeks gestation **or** a weight of less than 350 grams.

Section 36-339. Reproduction of Records. Amended to provide for electronic or other reproductions of certificates and to authorize disposal of records by regulation.

Section 36-346 Repealed. New Section 36-346 Added. The penalty provisions have been strengthened to serve as a deterrent to illegal use of vital records and to provide adequate penalties when prosecution is necessary.

IT WAS MOVED AND CARRIED TO OFFER GENERAL SUPPORT TO THE PROPOSED LEGISLATIVE CHANGES IN THE MODEL STATE VITAL STATISTICS ACT.

MATERNAL DEATHS

Dr. William A. Susong, Chairman of the Section on Maternal Mortality of the Maternal & Child Health Care Committee of this Association requested the Committee to introduce and support, during the 1979 Legislative session, a bill requiring reporting of maternal deaths by all hospitals throughout the state.

IT WAS MOVED AND CARRIED TO INTRODUCE AND ACTIVELY SUPPORT LEGISLATION PROVIDING FOR REQUIREMENTS TO REPORT MATERNAL DEATHS BY ALL HOSPITALS THROUGHOUT THE STATE.

CRIPPLED CHILDREN'S PROGRAM

Dr. Dandoy explained that the budget for the Department of Health Services, for fiscal year 1978-79, did not include sufficient funds to operate the Crippled Children's Program and that services have necessarily been limited to emergency care only. Staff is preparing legislation currently to provide for some supplemental appropriations to provide services for the rest of the year.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT NECESSARY APPROPRIATIONS FOR THE CRIPPLED CHILDREN'S PROGRAM

MANDATORY SEAT BELT RESTRAINTS

Dr. Chisholm requested introduction and active support by the Committee of legislation proposed by the Arizona Chapter, American Academy of Pediatrics requiring every person residing in this state transporting a child under the age of four (4) to provide for protection of the child with a child passenger restraint system meeting the federal motor vehicle safety standards. Provided further that the term "motor vehicle" as used in this paragraph shall not apply to trucks having a tonnage totaling of one ton or more. Provided that in no event shall failure to wear a child passenger restraint system be considered negligence nor shall such failure to wear said child passenger restraint system be admissible as evidence in the trial of any civil action. Violation of above subsection shall incur a fine of not less than two dollars ($2.00) nor more than ten dollars ($10.00) for each violation.

IT WAS MOVED AND CARRIED TO INTRODUCE AND ACTIVELY SUPPORT LEGISLATION PROVIDING FOR CHILD AUTO SAFETY SEAT RESTRAINTS.

OPTOMETRY - USE OF DIAGNOSTIC AGENTS

Dr. Moore informed the Committee that he anticipates introduction of legislation which would provide that diagnostic pharmaceutical agents authorized by the Board of Optometry may be used in the practice of optometry. The Committee was urged to actively seek defeat of such legislation.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT LEGISLATION PROVIDING FOR THE USE OF DIAGNOSTIC AGENTS IN THE PRACTICE OF OPTOMETRY.

PODIATRY - MANDATING HOSPITAL PRIVILEGES

The Committee was informed that legislation may be introduced which would mandate health care institutions to provide staff privileges for Podiatrists. The Committee was urged to actively seek defeat of such legislation.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT LEGISLATION PROVIDING FOR THE MANDATING OF HEALTH CARE INSTITUTIONS TO PROVIDE STAFF PRIVILEGES FOR PODIATRISTS.

MANDATORY MATERNITY COVERAGE

Dr. Sattesnpiel reminded the Committee that in previous years the Association had introduced legislation that would provide for mandatory maternal benefits in all insurance contracts provided in the state of Arizona. The Society of OB-Gynecologists would appreciate the Association's support of such legislation again this year.

IT WAS MOVED AND CARRIED TO INTRODUCE AND GENERALLY SUPPORT LEGISLATION PROVIDING FOR THE MANDATING OF MATERNAL BENEFITS IN ALL INSURANCE CONTRACTS PROVIDED IN THE STATE OF ARIZONA.

EXECUTIVE COMMITTEE

The meeting of the Executive Committee of the Arizona Medical Association, Inc., held in the Apache Room of the Adams Hotel, at Central & Adams, Phoenix, Arizona, on Friday, December 15, 1978, a quorum being present, convened at 9:10 p.m., Richard L. Dexter, M.D., President and Chairman, presiding.

7TH AMA NATIONAL LEADERSHIP CONFERENCE

IT WAS MOVED AND CARRIED THAT WILLIAM E. CRISP, M.D., AS PRESIDENT-ELECT, AND JOHN T. CLYMER, M.D., AS VICE PRESIDENT, BE REQUESTED TO ATTEND, AT THE ASSOCIATION'S EXPENSE, THE 7TH AMA NATIONAL LEADERSHIP CONFERENCE SCHEDULED TO BE HELD AT THE DOWNTOWN MARRIOTT HOTEL IN CHICAGO FEBRUARY 15-18, 1979.

IMPERIAL INSURANCE COMPANY

Mr. Jacobson addressed the committee regarding the recent request for a legal opinion concerning Imperial Insurance Company's liquidation, the statutes as they pertain to retroactive inclusion of professional liability in the Arizona Property and Casualty Insurance Guaranty Fund, and the participation in any way by the Association on behalf of its members who may become involved in litigation as a result thereof. Mr. Jacobson advised that apparently about 900 members would be affected by any litigation/judgment and that he had discussed the matter in depth with Roger Mitten, legal counsel presently representing Walter R. Eicher, M.D., one of those 900 members. Following a lengthy discussion by the committee, it was agreed that the Association would participate only by way of communication to its members of the fact that such situation exists, that those members involved should be aware of and prepare for a possible loss, and that the Association is in sympathy with the endeavor with which they are faced. The committee requested Mr. Jacobson to again contact Roger Mitten to determine the best time for such contact with the membership.

Future Medical Meetings

CONTINUING MEDICAL EDUCATION

The following institutions and organizations have been accredited for their continuing medical education programs by the Liaison Committee on Continuing Medical Education.

Arizona Heart Institute
Arizona Medical Association, Inc.
Arizona State Hospital, Phoenix
Desert Samaritan Hospital, Mesa
Good Samaritan Hospital, Phoenix
Health Maintenance Associates
Phoenix Indian Medical Center
Phoenix Psychiatric Council
Maricopa County General Hospital, Phoenix
Memorial Hospital, Phoenix
St. Luke's Hospital & Medical Center, Phoenix
St. Joseph's Hospital & Medical Center, Phoenix
Tucson Hospitals Medical Education Program, Tucson
U of A College of Medicine
Veterans Administration Center, Prescott
Veterans Administration Hospital, Phoenix

The accredited institutions and organizations above produce a variety of continuing medical education programs. Each accredited institution and organization is responsible for designating which of these programs meet ArMA's requirements for Category 1 credit. Physicians who participate in programs which are designated Category 1 by accredited institutions will receive Category 1 credit toward the ArMA Certificate in CME and the AMA's Physician's Recognition Award.

FEBRUARY

Second Annual Postgraduate Course In OB/GYN
February 14-16, 1979, Scottsdale Hilton Hotel, Scottsdale, AZ. Sponsors: Phoenix OB/GYN Society and Dept. of OB/GYN Maricopa County General Hospital. Contact: Secretary, Phoenix OB/GYN Society, 333 E. Virginia, Ste. 222, Phoenix, AZ 85004, (602) 257-9218. Approved for category 1 credit.

Advanced Cardiac Life Support Programs Provider Course
February 16 & 17, 1979. Arizona Medical Association, Inc., 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Association. Contact: Carol Turner at the Arizona Medical Association. Approved for 16 hours of category 1 credit.

Health Policy and Chronic Illness: The National Debate
February 17 & 18, 1979. Sherton-Place Hotel, San Francisco, CA. Sponsor: University of California, San Francisco Schools of Medicine. Contact: Ms. Bruce, University of California, San Francisco Continuing Education in Health Sciences, 1343 3rd Ave., San Francisco, CA 94143.

Ultrasound Meeting
February 19, 7—9 p.m. Medical Education Bldg., Good Samaritan Hospital. Sponsor: Good Samaritan Hospital. Contact: Avi Ben-Ora, M.D., 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 2 hours category 1 credit per session.

International Cardiovascular Congress II Non-Invasive Diagnosis
February 19,20,21, 1979. Scottsdale Center for the arts, Scottsdale, AZ. Sponsor: Arizona Heart Institute. Contact: Arizona Heart Institute, P.O. Box 10,000. Phoenix, AZ 85064. Approved for 17 hours of category 1 credit.

16th Annual Meeting of the Federation of Western Societies of Neurological Science
February 22—25, 1979. Mountain Shadows Resort, Scottsdale, AZ. Sponsor: College of Medicine, U of A & Western Soc. of Neurological Science. Contact: Lawrence Z. Stern, M.D., U of A Health Sciences Center, Dept. of Neurology, Tucson, AZ 85724. Approved for 18 hours of category 1 credit.

Alcoholism Awareness Week
February 19—25, 1979 has been declared by Governor Babbitt. Special activities will be occurring leading up to and during this week.

Advances In Internal Medicine
February 22-24, 1979, Casa Blanca Inn, Scottsdale, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

1979 Annual Scientific Meeting: Arizona Society of Anesthesiologists
February 24,25,1979. Radisson Scottsdale Resort, 7601 E. Indian Bend Rd., Scottsdale, AZ. Sponsor: College of Medicine, Tucson, AZ & Arizona Society of Anesthesiologists. Approved for 10 hours of category 1 credit.

Medical Progress: A review of Advances In Medicine In Past 5 Years
February 22-24, 1979, Casa Blanca Inn, Scottsdale, AZ. Sponsor: Maricopa County General Hospital. Contact: Medical Education Office, Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 15 hours of category 1 credit.

MARCH

Day of G.I. & Liver Disease
March 2, 1979. Camelback Inn, Scottsdale, AZ. Sponsor: St Joseph's Hospital and Medical Center. Contact: Ethelann Murray, M.D., St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Approved for 6 hours of category 1 credit.

New Mexico Metabolism Symposium
March 8, 9, & 10, 1979, Taos, New Mexico. Contact: Office of Education, Lovelace Medical Center, Albuquerque, New Mexico. (505) 842-7353.

Ultrasound Meeting
March 8, 7—9 p.m., Medical Education Bldg. Good Samaritan Hospital. Sponsor: Good Samaritan Hospital. Contact: Avi Ben-Ora, M.D., 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 2 hours of category 1 credit per session.

1979 National Medicolegal Symposium
March 8—11, 1979. Caesars Palace Hotel, Las Vegas, Nevada. Sponsors: American Medical Assoc. and American Bar Assoc. Contact:

American Medical Association, 535 N. Dearborn St., Chicago, Ill 60610. Approved for category 1 credit.

Advanced Cardiac Life Support Programs Instructor Course
March 23 & 24 1979. Arizona Medical Assoc., Inc., 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner at the Arizona Medical Association. Approved for 16 hours of category 1 credit.

Purgatory Colorado Medical Ski Symposium
March 8 — 11, 1979. Ramada Inn, Durango, Co. Sponsor: Albuquerque Academy of Family Physicians. Contact: Albuquerque Academy of Family Physicians, 2650 Yale, S.E., No. 10, Albuquerque, N.M. 87105. Approved for 12 hours of category 1 credit.

Psychopharmacology In Children
March 9—11, 1979, Double Tree Inn, Tucson, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

Clinical Recognition and Management of Heart Disease — 1979
March 22,23 & 24, 1979. U of A Health Sciences Center, Main Auditorium. Sponsor: U of A College of Medicine. Contact: Registrar, American College of Physicians, 420 Pine St., Philadelphia, PA 19104.

Third Annual Southwestern Cardiovascular Symposium — 1979
March 28, 29, & 30, 1979. The Reistry Resort, Scottsdale, AZ. Sponsor: St. Luke Hospital Medical Center, 525 N. 18th St. Phoenix, AZ 85006. Contact: Public Relations, St. Luke's Hospital. Approved for 14 hours of category 1 credit.

Second International Conference on the Adjuvant Therapy of Cancer
March 28—31, 1979. Tucson Convention Center, Tucson, AZ. Sponsor: U of A College of Medicine, Cancer Center Division. Contact: Cancer Center Division, U of A College of Medicine, Tucson, AZ 85724. Approved for 23 hours of category 1 credit.

Second Annual Symposium on Aging
March 31 and April 1, 1979. Sheraton-Place Hotel, San Francisco, CA Sponsor: Univ. Of California, San Francisco Schools of Medicine. Contact: Ms. Bruce, Univ. of California, San Francisco Continuing Education in Health Sciences, 1343 3rd Ave, San Francisco, CA 94143. Approved for category 1 credit.

APRIL

Fifteenth Annual Arizona Chest Symposium
April 6,7,8, 1979. Doubletree Inn, Tucson, AZ. Sponsor: College of Medicine, U of A and Tucson Medical Center. Contact: Linda Alpert, R.N., Symposium Coordinator Tucson, Medical Center, P.O. Box 6067, Tucson, AZ 85733. Approved for category 1 credit.

Health Hazard Appraisal: Clinical Information for Consumer and Practitioners
April 21 & 22, 1979. Sherton-Place Hotel, San Francisco, Ca. Sponsor: University of California, San Francisco. Contact: Ms. Bruce, Univ. of California, San Francisco, Continuin Education Health Sciences, 1343 Third Ave., San Francisco, CA 94143

88th Annual Meeting: Arizona Medical Association
April 25—29, 1979. Sponsor: Arizona Medical Association, Inc. Contact: Bruce E. Robinson, Executive Director, 810 W. Bethany Home Rd., Phoenix, Z 85014. Approved for category 1 credit.

MAY

Fourth Annual Update: Primary Care
May 2—5, 1979, Arizona Health Sciences Center Tucson, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

MONTHLY OR WEEKLY

Shrine Medics Meeting
Second Tuesday of each month, Doctors Hospital, 5:45 p.m. J. South Classroom. Sponsor: Shrine Medics. Contact: Robert C. Briggs, M.D., 5121 N. Central Ave., Phoenix, AZ 85012.

Office Psychiatry for the Primary Provider
2nd Monday of month, 4811 N. 7th Street, Phoenix, AZ. Sponsor: Arizona Health Plan. Contact: T.R. Bittker, M.D., Box 5000, Phoenix, AZ 85010. Approved for category 1 credit.

Counter Transference Group
Weekly, Thurs. 8—10 p.m. Sponsor: Phoenix Psychiatric Council. Contact: James E. Campbell, M.D., 5051 N. 34th St., Phoenix, AZ 85018. Approved for 2 hours category 1 credit.

Monthly Meeting of Tucson Radiologists
Last Tues. of month. Plaza International, Tucson, AZ. Sponsor: U of A Medical Center, Dept. of Radiology. Contact: Irwin M. Freundlich, M.D., U of A Health Sciences Center, Dept. of, Radiology, Tucson, AZ 85724. Approved for 2 hours category 1 credit.

Pediatric Grand Rounds
Tuesday 7:30-8:30 a.m in Phoenix: 1st Tues.—Phoenix Indian Hospital, 2nd Tues.—Maricopa County Hospital, 3rd Tues.—Good Samaritan Hospital, 4th Tues.—St. Joseph's Hospital. Sponsor: Maricopa County Hospital (Phoenix Hospital's Affiliated Pediatric Program). Contact: J. Kipp Charlton, M.D., 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

Review of Forensic Pathology Current Case, Special Topics
Thursday, weekly, 11 a.m., 120 S. 6th Ave., Phoenix, AZ. Sponsor: Arizona Society of Pathologists. Contact: H.H. Karnitschnig, M.D., 120 S. 6th Ave., Phoenix, AZ. Approved for 1 hour per session category 1 credit.

Staff Education Conference
Wednesdays, weekly, 1 p.m., Arizona State Hospital, Phoenix, AZ. Sponsor: Arizona State Hospital. Contact: Howard E. Wulsin, M.D., Arizona State Hospital, 2500 E. Van Buren, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

BARROW NEUROLOGICAL INSTITUTE

Medical Education
Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Sponsor: St Joseph's Hospital & Medical Center. Contact: John R. Green, M.D. Approved for 1 hour category 1 credit.

Neurology Teaching Conference
Tuesdays, 8:30-9:30 a.m., Eighth Floor Conf. Room.

Neurosurgery Morbidity Conference
Wednesdays, 8:15-9:15 a.m., on first and third weeks, Eighth Floor Conference Room.

Neuro-ophthalmology Conference
Tuesdays, 7:30 a.m. in 8th floor neurology conference room.

Spinal Injury Conference
Wednesdays, 8:15-9:15 a.m., on second and fourth weeks, in Neuropathology Conf. Rm.—a multidisciplinary review of admission by neurosurgeons, orthopedists, and rehabilitation specialists

Neuropathology of Gross Specimens Conference
Thursday, 7:30-8:30 a.m. in the Morgue.

Neurology-Neurosurgical Clinical-Neuroradiological and Neuropathological Conference
Fridays, 8-9 a.m., First Floor Conference Rm.

Neuropathology or Neuroradiology Conferences
Friday, 9 a.m., Neuropathology in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

Neurorehabilitation Conference
Tuesdays, noon, 8th Floor Conference Rm.

Neurosurgical Journal Club
Saturdays, 9-11 a.m. in Eighth Floor Conference Rm.

CAMELBACK HOSPITAL

5055 N. 34th St., Phoenix, AZ 85018. Sponsor: Camelback Hospital. Contact: Medical Director.

Patient Staffing Conference
Three times weekly

DESERT SAMARITAN HOSPITAL

Wednesday evenings, 7 p.m. Sponsor: Desert Samaritan Hospital. Contact: L. A. Rosati, M.D., Laboratory, Desert Samaritan Hospital, Mesa, AZ 85202. Approved for category 1 credit.

Monthly Visting Professor Program
Tuesday Evenings at 7 p.m.

Surgical Morbidity & Mortality Conference
2nd Thursday, 7 a.m., Grande Room

Department of Medicine Clinical Conferences
Thursday, 12:30—1:30 p.m., Grande Room.

OB/GYN Clinical Conferences
Monday, 12:30—1:30 p.m., Grande Room.

GOOD SAMARITAN HOSPITAL

Clinical Cancer Conference
3rd Wednesday, every month, Butler Bldg. Conference Rm. Good Samaritan Hospital. Contact: John A. Bruner, M.D., 926 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour per session category 1 credit.

Pulmonary Disease Grand Rounds
Mondays, 12 Noon, D-5 North Conf. Rm., Good Samaritan Hospital, Phoenix, AZ. Sponsor: Pulmonary Disease Teaching Service, Good Samaritan Hospital. Contact: Bernard E. Levine, M.D., Pulmonary Function Laboratory, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour category 1 credit.

MARYVALE SAMARITAN HOSPITAL

Continuing Medical Education Program
Maryvale Samaritan Hospital, every other Wednesday, 7-8 a.m., January 25, 1978

MARICOPA COUNTY GENERAL HOSPITAL

2601 E. Roosevelt, Phoenix, AZ 85008. Sponsor: Maricopa County General Hospital. Contact: H. F. Lenhardt, M.D., Dir. of Medical Education. Approved for category 1 credit.

Recent Advances in Geriatric Psychiatry
January 20, 1979. Maricopa County General Hospital

5th Annual MCGH Urological Seminar
January 27 & 28, 1979. Doubletree Inn, Scottsdale, AZ 85251.

Current Advances in Obstetrics and Gynecology
February 14, 15 & 16, 1979, Scottsdale Hilton Hotel, Scottsdale, AZ.

Medical Progress: A Review of Advances in Medicine in the Past 5 Years
Feb. 22, 23 &, 24, 1979. Carefree Inn, Carefree, AZ 85331.

The Head
Presented by Dept. of Radiology, Feb. 9, 10 11, 1979. Doubletree Inn, Scottsdale, AZ 85251

MEMORIAL HOSPITAL

1201 S. 7th Ave., Phoenix, AZ 85036. Sponsor: Memorial Hospital. Approved for category 1 credit.

Month Medical Education Seminar
Third Monday, 6:30 p.m., Kiva Conference Rm. Contact: George Scharf, M.D.

Tumor Board Conference
Every Friday at Noon, Kiva Conference Rm. Contact: Howard Kimball, M.D.

SCOTTSDALE MEMORIAL HOSPITAL

7300 E. 4th St., Scottsdale, AZ 85251. Sponsor: Scottsdale Memorial Hospital. Contact: W. S. Wiliams, M.D., Director of Medical Education

Clinical Pathological Conference
4th Monday, monthly, 12:45 p.m.

Family Practice Conference
1st Monday, monthly, 12:45 p.m.

Medical Grand Rounds
3rd Monday, monthly, 12:45 p.m.

Morbidity & Mortality Conference
2nd Monday, monthly, 12:45 p.m.

ST MARY'S HOSPITAL & HEALTH CENTER

1601 W. St. Mary's Rd., Tucson, AZ 85703. Sponsor: St. Mary's Hospital & Health Center. Contact: see below.

Cardiology Conference
Every Friday 8-9 a.m., Century Rm. A. Contact: Anthony L. Forte, M.D.

Monthly Specialty Conference of the Department of Surgery
First Monday, monthly, 7:30 a.m. Century Rm. A. Contact: Medical Staff Office. Approved for 1 hour of category 1 credit

Grand Rounds: Medical Surgical, Family Practice, Pathology, Radiology
Weekly, Thursday, 7-8:30 a.m. Contact: Richard A. Silver, M.D. Approved for 1 hours of category 1 credit.

U OF A HEALTH SCIENCES CENTER

Sponsor: U of A College of Medicine, Tucson, AZ 85724. Contact: See below. Approved for category 1 credit.

Clinical Immunology, Allergy & Rheumatology Rounds
Every Friday, Noon-1 p.m. Contact: John Boyer, M.D., Dept. of Internal Medicine.

Cerebrovascular Disease Conference
Mondays, 5-6 p.m., weekly, Rm. 5505. Contact: Wesly Moore, M.D.,Depts. of Surgery, Nurology & Radiology.

Dean's Clinical Rounds
October 18, 1978, Main Auditorium, UAHSC. Contact: Louis J. Kettel, M.D.

Endocrinology Seminar
Every Thursday, Noon-1 p.m., 1st, 3rd & 5th Thursday, Room N318, VA Hospital. 2nd & 4th Thursday, Room 6505, Tucson Medical Center. Contact: Dept. of Internal Medicine.

Hematology-Oncology Clinical Conference
Every Tuesday, Noon-1 p.m., 1st, 3rd & 5th Tuesdays, Rm 6505, Tucson Medical Center. 2nd & 4th Tuesdays, Rm. N318, VA Hospital. Contact: Sidney Salmon, M.D., Dept. of Internal Medicine.

Joint Thyroid Clinic Conference
1st & 3rd Wednesdays of every month. AHSC, Rm. 6505. Contact: Sidney Werner, M.D., Dept. of Internal Medicine, Endocrinology Section.

Medical Grand Rounds
Every Wed., Noon-1p.m., 1st, 3rd, & 5th Wed., Staff Conf. Room, VA Hospital. 2nd & 4th Wed.,Rm. 5403, UAHSC. Contact: Jay Smith, M.D., Dept. of Internal Medicine.

Nuclear Medicine
Thursday, 7:30 a.m., Radiology Conf. Rm., UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Diagnostic Radiology.

Neurology Grand Rounds
/Every Friday, Noon, 1st, 3rd, & 5th Fridays, UAHSC, Rm. 7505. 2nd & 4th Fridays, VA Hospital. Contact: William A. Sibley, M.D., Dept. of Neurology.

Neuropathology Review Conference
Thursdays, 8:30 a.m., Rm. 5120, UAHSC. Contact: Peter C. Johnson, M.D.

Neurosciences Seminar
Every Friday, 7:30 a.m.,UAHSC, Rm 7505. Contact: Colin R. Bamford, M.D., or Jose F. Laguna, M.D., Dept. of Neurology.

Pathology Seminar
Friday, 4:30-5:30 p.m., Rm. 5120, UAHSC. Contact: Paul Finley, M.D., Dept. of Pathology.

Tucson Pathologist Conference
First Monday of the Month, 7:30-9 p.m. Rotation between Tucson Pathology Conf. Rms. Contact: Anna Graham, M.D., Tucson Pathologists.

Pediatric Grand Rounds
Every Tuesday, 12:30-1:30 p.m. Alternates between Tucson Medical Center & UAHSC. Contact: Hugh Thompson, M.D., Dept. of Pediatrics.

Problem Case Workshop
3rd Monday of each month, 7:30 a.m., Rm 4410, UAHSC. Contact: H. E. Cross, M.D., Ph.D., Div. Of Ophthalmology.

Psychiatric Grand Rounds
Every Wednesday, Sept. to May 4, 5:30 p.m., Rm8403 UAHSC. Contact: Alan Levenson, M.D., Dept. of Psychiatry.

Chest Radiology
Monday, 5-6 p.m., weekly, Rm 1535F, UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

STANFORD UNIVERSITY SCHOOL OF MEDICINE
OFFICE OF POSTGRADUATE MEDICAL EDUCATION

presents

BASIC SCIENCE FOR CLINICIANS

AT STANFORD UNIVERSITY
FEBRUARY 26-MARCH 2, 1979

This five-day multidisciplinary course is a concise but comprehensive review of basic medical science designed to meet the needs of those clinicians who wish to expand their knowledge of molecular biology. Early registration is advised as attendance is limited. Tuition fee of $290 is payable upon application for enrollment.

General lectures will cover a review of chemistry and physics for clinicians, chemical bonds of biological importance, subatomic particles, correlation of cell structure and function, the structure and function of proteins, sugars and lipids, the structure of nucleic acids, DNA synthesis, expression and organization of genetic information, regulation of gene expression, gene manipulation, carbohydrate and fat metabolism, bioenergetics, membrane structure, the organization and function of the brain.

Elective sessions will include the evolution of proteins, the discovery of particles with charm, bacterial antibiotic resistance, structure and function of heterochromatin, cellular and humoral mechanisms of immunity, human evolution, mediators of inflammation and immunity, mitochondria and related diseases, nutrition, association between HL-A and various disease states, nerve growth factors, demonstration of electric signalling by nerve cells.

A faculty of 18 Stanford University biomedical scientists, including three Nobel Laureates, will take part in the program.

BASIC SCIENCE FOR SURGEONS

AT DEL MONTE LODGE, PEBBLE BEACH
MARCH 11-13, 1979

This course provides an in-depth review of some important changes in basic surgical science. Discussions will focus both on basic principles and practical applications and will cover body fuels and surgical nutrition, receptors and disease, and blood gas and acid-base problems.

Tuition fee is $125. Early application is advised.

CLINICAL ASPECTS OF HYPERTENSION

AT STANFORD UNIVERSITY
MARCH 17, 1979

This one-day seminar will cover the hazards of hypertension; office work-up of the hypertensive patient; goals in therapy; renin, aldosteron and hypertension; action of anti-hypertensive drugs; and office management of hypertension. It is intended for all physicians who deal with problems related to hypertension. Tuition fee is $30 and advance registration is required.

The Postgraduate Medical Education program at Stanford University School of Medicine is fully accredited by the Council on Medical Education of the American Medical Association and approved for Category I Credit toward the California Medical Association's Certificate in Continuing Education. Application has been made for AAFP credit. Attendance certificates are provided.

Director of Courses: Edward Rubenstein, M.D.

Early application is advised

Clip and mail to
OFFICE OF POSTGRADUATE MEDICAL EDUCATION
Stanford University School of Medicine, Room TC-129, Stanford, California 94305 / Telephone (415) 497-5594

ENROLL ME IN ________ **Therapy** ($290 enclosed); ________ **Basic Science for Clinicians** ($290 enclosed);
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Gastrointestinal Radiology
Mondays, 7:30 a.m., weekly except for summer months. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Radiation Oncology Planning Conference
Friday, weekly, 8:30-10 a.m., UAHSC, Rm. 0655. Contact: Robert S. Heusinkveld, M.D., Radiation Oncology Section.

Radiology-Rheumatology Conference
Thursday, 8 a.m., UAHSC, Library Rm. 1535C. Contact: Irwin M. Freundlich, M.D. Dept. of Radiology.

Vascular Radiology
Radiology Interesting Case Conference
Thursday, Noon, VA Hospital. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Resident's Conference
Wednesday, weekly 5-6 p.m., Diag. Radiology Conf. Rm. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology

Trauma Conference
Every Thursday, 4-5 p.m. UAHSC, Rm. 5505. Contact: Martin Silverstein, M.D., Dept. of Surgery.

Grand Ward Rounds—Trauma
Every Tuesday, 8 a.m., UAHSC. Contact: Martin Silverstein, Surgery Dept., Trauma Section.

Monthly Meeting Tucson Ultrasonography Group
First Wed. of month, 4:30-5:30 p.m., UAHSC. Contact: Irwin M. Freundlich, M.D.

Tucson Urological Society Scientific Meeting
Monthly. Contact: George W. Drach, M.D., Depts. of Surgery & Urology.

General Urology Conference
Tuesday 5-6 p.m. Thursday, Noon-1:30 p.m. UAHSC Meeting Rooms & VA Hospital. Contact: George W. Drach, M.D., Dept of Surgery/Urology Section.

VETERANS ADMINISTRATION HOSPITAL

7th St. and Indian School Rd., Phoenix, AZ 85012. Sponsor: VA Hospital. Contact: Jasper L. McPhail, M.D. Approved for Category 1 credit.

Academic Surgery Conference
Each Thursday — 2 p.m. — C435, Dr. Cannon, Ext. 493.

Cardiology Conference
2nd Thursday — 1 p.m. — T5, Dr. Habibzadeh, Ext. 348.

Cancer Symposium
Each Wednesday — 1 p.m. — T5, Dr. Berkley, Ext. 419.

Clinical Conference
4th Thursday of 3rd Month, (Mar. Jun., Sept., & Dec.), 1 p.m. — T5, Dr. Likos, Ext. 623.

Dermatology Conference
1st, 2nd, & 3rd Wednesday (usually, but is subject to change) 10 a.m. — C118, Dr. Roberts, Ext. 426.

G.I. Radiology Clinical Correlation Conference 1st & 3rd Monday —1 p.m. — C435, Dr. Sanowski, Ext. 618.

G.I. Grand Rounds
Ech Tuesday — 1 p.m. — T5, (4th Thursday with U of A Consultants) Dr. Sanowski, Ext. 618.

Medical Service Grand Rounds
Each Friday — 11 a.m. — T5, Dr. Zeller, Ext 272

Medical-Surgical Chest Conference
1st and 3rd Thursday — 1 p.m. — T5, Dr. Chowdhury, Ext. 388.

Medical-Surgical G.I. Conference
Ist & 3rd Friday — 2 p.m. — 2123, Dr. Sanowski, Ext. 618.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery-Pathology Conference
Each Thursday — 2 p.m. — 2128, Dr. Cannon, Ext 493, & Dr. Likos, Ext. 623.

Urology-Pathology Conference
Each Wednesday — 7 a.m. — 2128, Dr. Likos, Ext. 623 & Dr. Pentenney, Ext., 417.

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JOINT LIFE INSURANCE

insures two people with only one policy, one low premium

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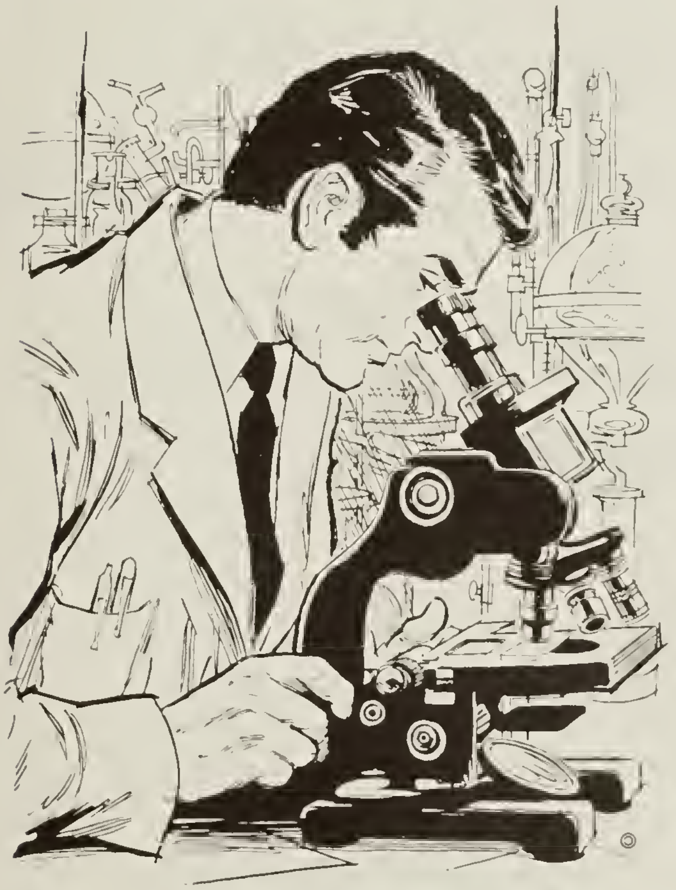
BUSINESS INSURANCE: Two doctors, partners or associates in a professional corporation, will find this plan a low-cost way to provide funds if one of the two dies. It also may be used by husband and wife or father and son to provide funds to pay off special debts or for any of the other purposes for which life insurance may be used.

LOWER INSURANCE AGE: Often, one insured is somewhat younger than the other. The joint equal age can take years off the age of the older insured. The policy provides for the payment of the face amount upon the death of the first of the two insureds to die.

GUARANTEES SURVIVOR INSURABILITY: The surviving insured, within 90 days and prior to age 70, is guaranteed the right to purchase life insurance. If the surviving insured doesn't exercise this right and dies during this 90-day period, the conversion would automatically be made by the Company and the face amount, less the conversion premium, would be paid to his beneficiary.



DOUBLE FOR SIMULTANEOUS DEATH: If both insureds should die simultaneously, the sum insured upon their deaths would be paid to their beneficiaries.

CONVERTIBLE TO SINGLE LIFE: The Joint Life Insurance may also be converted to single insurance prior to the older insured's 60th birthday. The amount converted can be all on one life or the other or divided between the two as long as each does not take less than $1,000 of life insurance.

An HBA Life Agent would be glad to discuss it further at your convenience.

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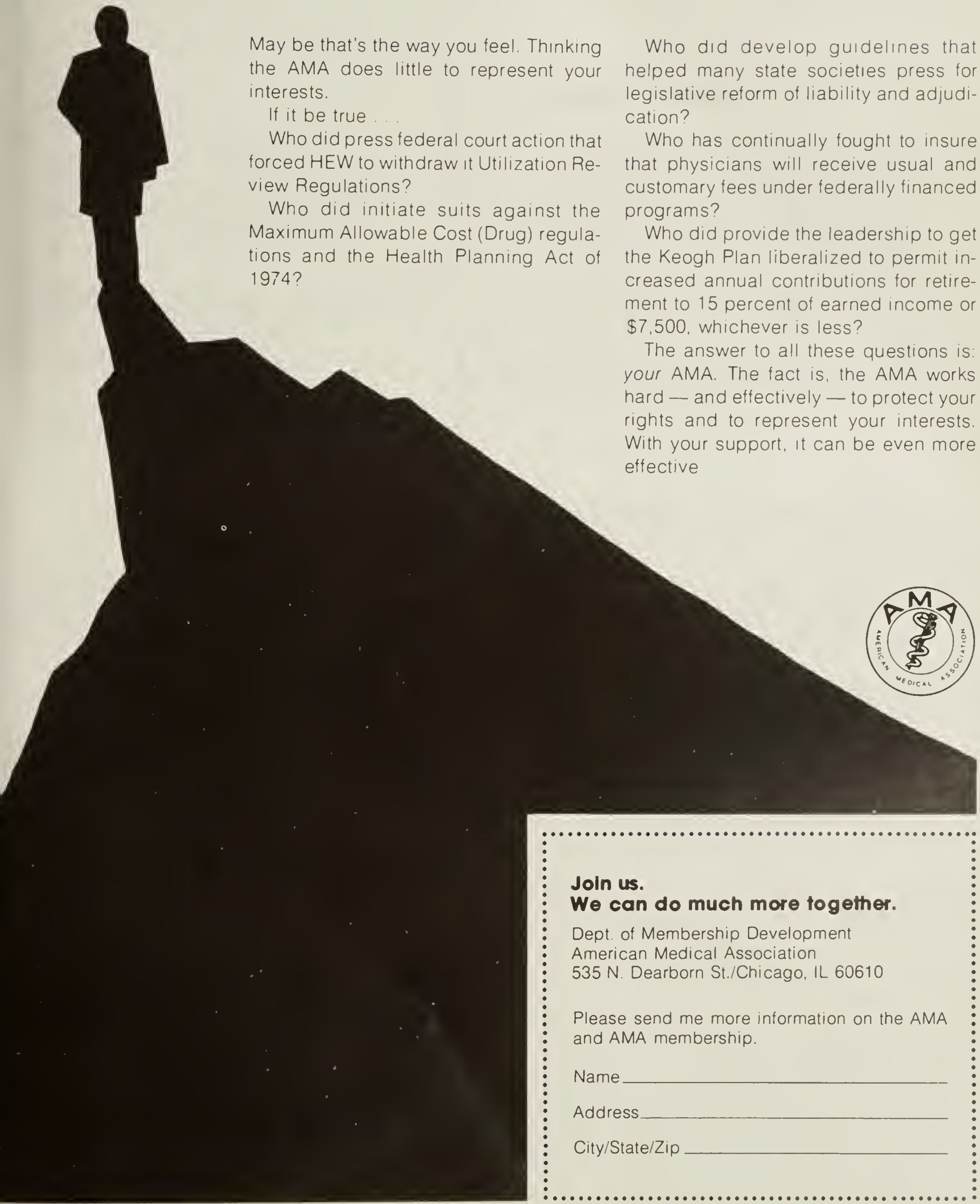

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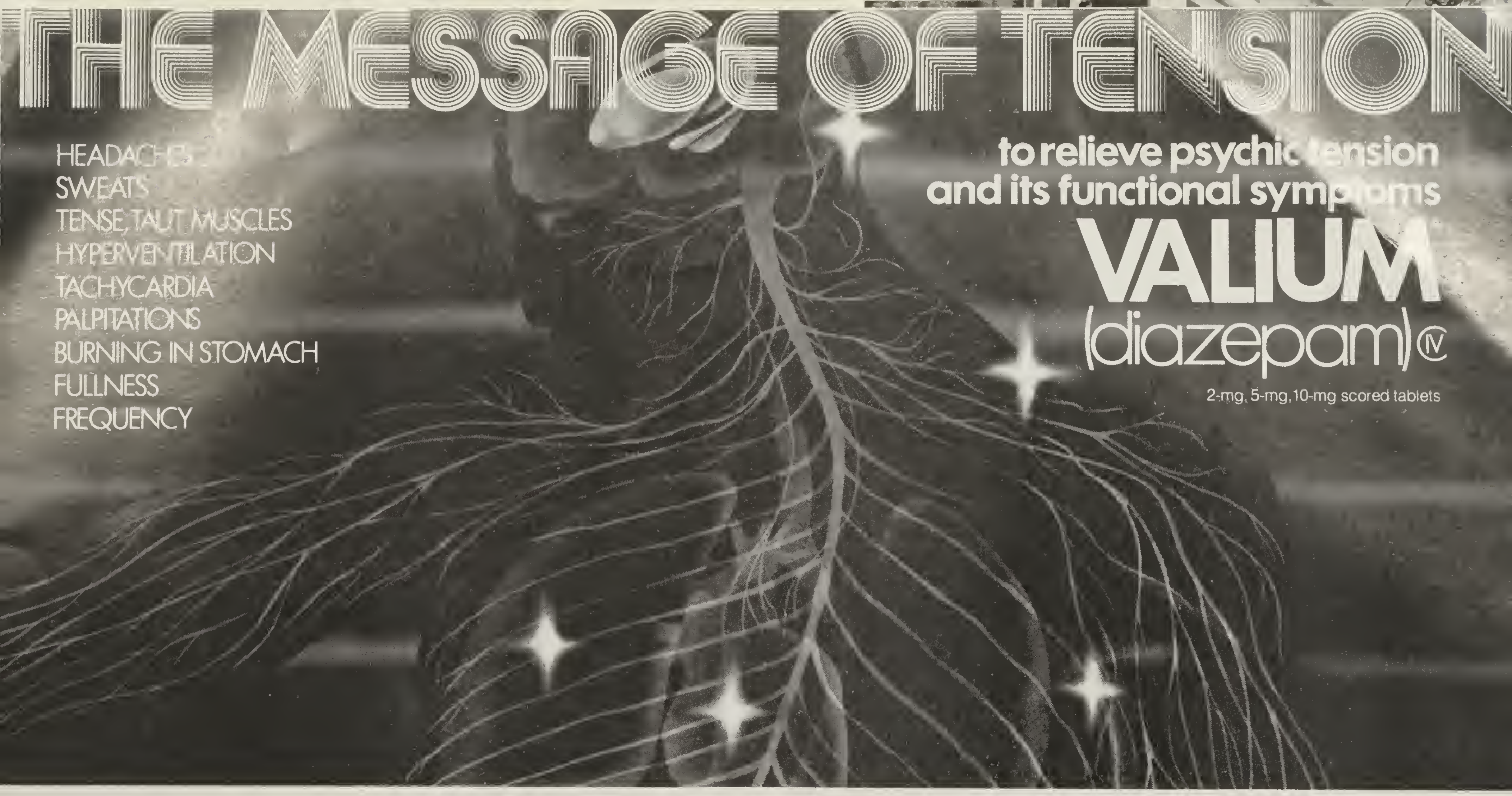

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Usage in Pregnancy: **Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**
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Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy

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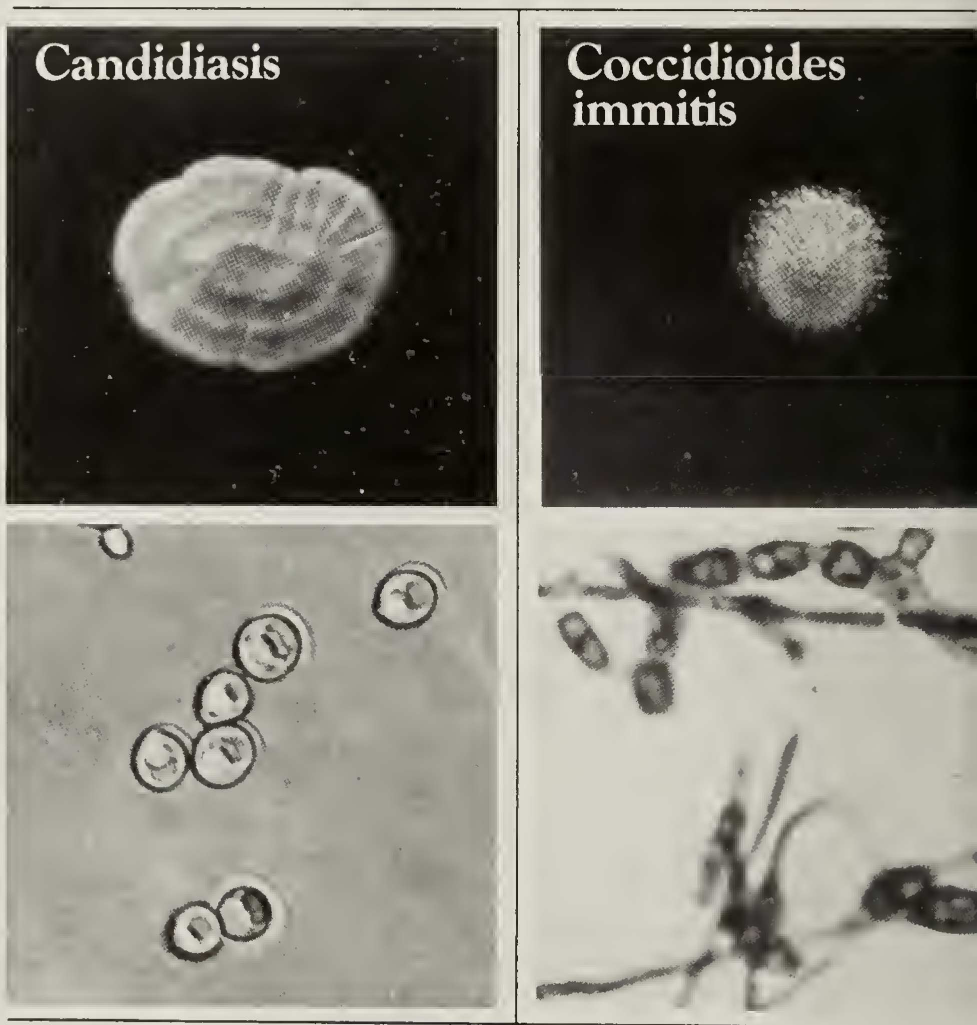

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and the side effect profile

no nephrotoxicity or other permanent adverse effects in clinical studies

- even in prolonged therapy
- even in patients with renal disease

extensively evaluated

During clinical trials in over 400 patients, no permanent adverse reactions were reported.

Adverse reactions

MONISTAT i.v. should not be administered undiluted. Rapid injection of the undiluted solution may produce transient tachycardia or arrhythmia.

Adverse reactions include phlebitis, pruritus, rash, nausea, vomiting, febrile reactions, drowsiness, diarrhea, anorexia and flushes. Transient hematologic changes have occurred; therefore, the patient should be closely monitored.

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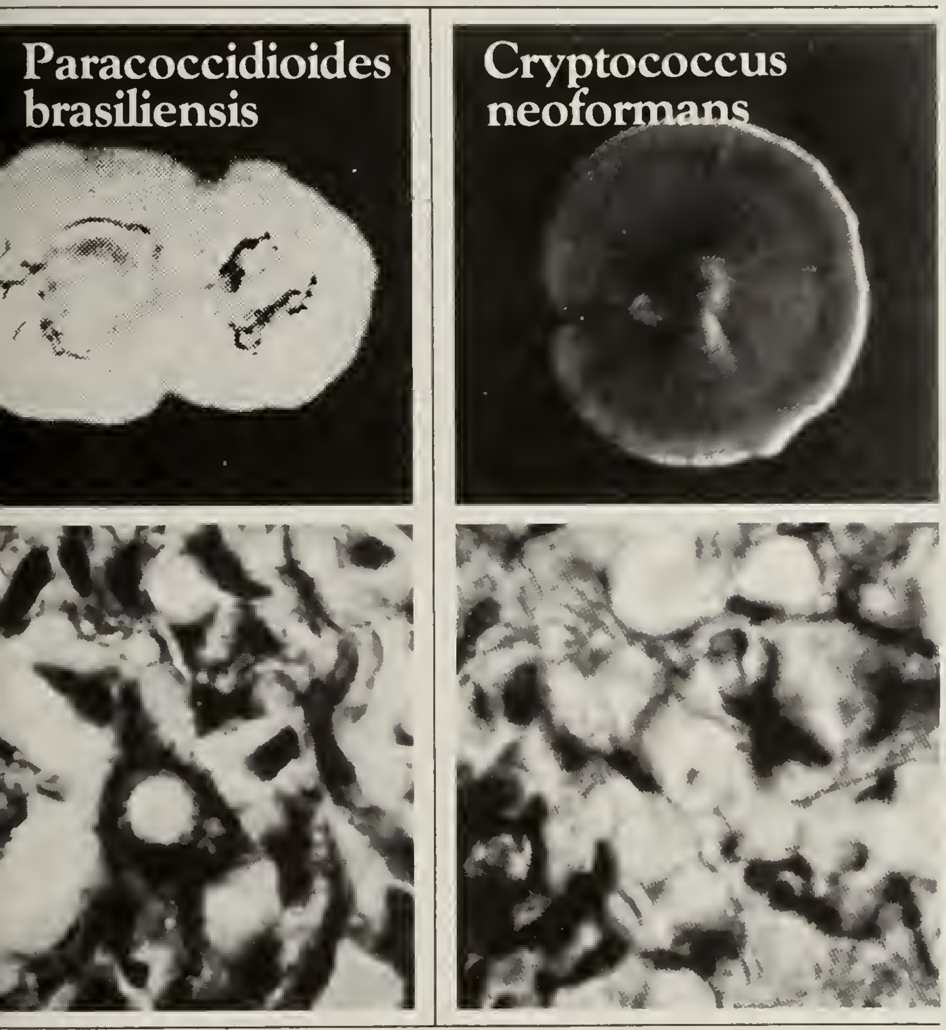
advancement systemic mycoses



generally well tolerated by severely debilitated patients

- cancer patients
- patients receiving immunosuppressive drugs
- patients with serious underlying conditions such as renal insufficiency or diabetes mellitus

for more information

Because of the uniqueness of new MONISTAT i.v. only some of the highlights can be presented in this advertisement. For more information, i.e., product monograph, dosage schedules, etc., please fill out the coupon on the next page and mail to Ortho Pharmaceutical Corporation.

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new Monistat i.v.

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(miconazole)

broad-spectrum activity against major systemic fungal pathogens

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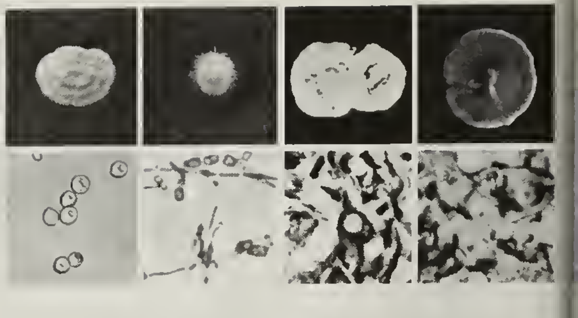

a broad-spectrum systemic antifungal agent

DESCRIPTION: MONISTAT i.v. (miconazole) 1-{2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl) methoxyl ethyl} 1 H-imidazole is a synthetic antifungal supplied as a sterile solution for intravenous infusion. Each ml of this solution contains 10 mg of miconazole with 0.115 ml PEG 40 castor oil, 1.0 mg lactic acid USP, 0.5 mg methylparaben USP, 0.05 mg propylparaben USP in water for injection. Miconazole i.v. is a clear, colorless to slightly yellow solution having a pH of 3.7 to 5.7.

CLINICAL PHARMACOLOGY: MONISTAT i.v. is rapidly metabolized in the liver and about 14% to 22% of the administered dose is excreted in the urine, mainly as inactive metabolites. The pharmacokinetic profile fits a three-compartment open model with the following biologic half-life: 0.4, 2.1, and 24.1 hours for each phase respectively. The pharmacokinetic profile of MONISTAT i.v. is unaltered in patients with renal insufficiency, including those patients on hemodialysis. The in/vitro antifungal activity of MONISTAT i.v. is very broad. Clinical efficacy has been demonstrated in patients with the following species of fungi: *Coccidioides immitis, Candida albicans, Cryptococcus neoformans,* and *Paracoccidioides brasiliensis.*

Recommended doses of MONISTAT i.v. produce serum concentrations of drug which exceed the in-vitro MIC values for the fungal species noted above. Doses above 9 mg/kg of MONISTAT i.v. produce peak blood levels above 1μg/ml in most cases. The drug penetrates into joints.

INDICATIONS: MONISTAT i.v. is indicated for the treatment of the following severe systemic fungal infections: coccidioidomycosis, candidiasis, cryptococcosis, paracoccidioidomycosis, and for the treatment of chronic mucocutaneous candidiasis. However, in the treatment of fungal meningitis and urinary bladder infections an intravenous infusion alone is inadequate. It must be supplemented with intrathecal administration and bladder irrigation. Appropriate diagnostic procedures should be followed and MICs should be determined.

MONISTAT i.v. should not be used to treat common trivial forms of fungal diseases.

CONTRAINDICATIONS: MONISTAT i.v. is contraindicated in those patients who have shown hypersensitivity to it.

WARNINGS: Rapid injection of undiluted MONISTAT i.v., may produce transient tachycardia or arrhythmia.

PRECAUTIONS: Before a treatment course of MONISTAT i.v. is started, the physician should make sure that the patient is not hypersensitive to the drug product. MONISTAT i.v. should be given by intravenous infusion. The treatment should be started under stringent conditions of hospitalization but subsequently may be given to suitable patients under ambulatory conditions with close clinical monitoring. It is recommended that an initial dose of 200 mg be given with the physician in attendance. It is also recommended that clinical laboratory monitoring including hemoglobin, hematocrit, electrolytes and lipids be performed.

It should be borne in mind that systemic fungal mycoses may be complications of chronic underlying conditions which in themselves may require appropriate measures.

Pregnancy: Reproductive studies with MONISTAT i.v. in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus. There are no data, however, on the use of the drug in pregnant women.

Children. Since the safety of miconazole i.v. in children under one year of age has not been extensively studied, its benefits in this age group must be weighed against the possible risks involved.

ADVERSE REACTIONS: Adverse reactions which have been observed with MONISTAT i.v. therapy include phlebitis, pruritus, rash, nausea, vomiting, febrile reactions, drowsiness, diarrhea, anorexia and flushes. In the U.S. studies, 29% of 209 patients studied had phlebitis, 21% pruritus, 18% nausea, 10% fever and chills, 9% rash, and 7% emesis. Transient decreases in hematocrit and serum sodium values have been observed following infusion of MONISTAT i.v. Thrombocytopenia has also been reported. No serious renal or hepatic toxicity has been reported. If pruritus and skin rashes are severe, discontinuation of treatment may be necessary. Nausea and vomiting can be mitigated with antihistaminic or antiemetic drugs given prior to MONISTAT i.v. infusion, or by reducing the dose, slowing the rate of infusion, or avoiding administration at mealtime.

Aggregation of erythrocytes or rouleau formation on blood smears has been reported. Hyperlipemia has occurred in patients and is reported to be due to the vehicle. Cremophor EL (PEG 40 castor oil).

DRUG INTERACTIONS: Drugs containing cremophor-type vehicles are known to cause electrophoretic abnormalities of the lipoprotein. These effects are reversible upon discontinuation of treatment but are usually not an indication that treatment should be discontinued.

Interaction with the coumarin drugs resulting in an enhancement of the anticoagulant effect has also been reported. In cases of simultaneous treatment with MONISTAT i.v. and coumarin drugs, the anticoagulant effect should be carefully titrated since reductions of the anticoagulant doses may be indicated.

DOSAGE AND ADMINISTRATION

DOSAGE

Adults. The doses may vary with the diagnosis and with the infective agent, from 200 to 1200 mg per infusion. The following daily doses, which may be divided over 3 infusions, are recommended:

Organism	Dosage Range*	Duration of Successful Therapy (weeks)
Coccidioidomycosis:	1800 to 3600 mg per day	3 to > 20
Cryptococcosis:	1200 to 2400 mg per day	3 to > 12
Candidiasis:	600 to 1800 mg per day	1 to > 20
Paracoccidioidomycosis:	200 to 1200 mg per day	2 to > 16

*May be divided over 3 infusions.

Repeated courses may be necessitated by relapse or reinfection.

Children: A total daily dose of about 20 to 40 mg/kg is generally adequate. However, a dose of 15 mg/kg body weight per infusion should not be exceeded.

ADMINISTRATION: MONISTAT i.v. should be diluted in at least 200 ml of fluid. The diluent of choice is 0.9% sodium chloride or alternatively Dextrose 5% injectable solution. The intravenous infusion should be given over a period of 30 to 60 minutes.

Generally, treatment should be continued until all clinical and laboratory tests no longer indicate that active fungal infection is present. Inadequate periods of treatment may yield poor response and lead to early recurrence of clinical symptoms. The dosing intervals and sites and the duration of treatment vary from patient to patient and depend on the causative organism.

OTHER MODES OF ADMINISTRATION: Intrathecal. Administration of the undiluted injectable solution of MONISTAT i.v. by the various intrathecal routes (20 mg per dose) is indicated as an adjunct to intravenous treatment in fungal meningitis. Succeeding intrathecal injections may be alternated between lumbar, cervical, and cisternal punctures every 3 to 7 days. Bladder instillation of 200 mg of diluted solution is indicated in the treatment of mycoses of the urinary bladder.

HOW SUPPLIED: MONISTAT i.v. is supplied in 20 ml ampoules.

MONISTAT i.v. (miconazole) is an original product of Janssen Pharmaceutica N.V., Belgium, and co-developed by Ortho Pharmaceutical Corporation.

Ortho

Ortho Pharmaceutical Corporation
Raritan, New Jersey 08869

Ortho Pharmaceutical Corporation **AM3—79**
c/o 733 Summer Street
Stamford, CT 06901

Please send me more information on the new broad-spectrum, systemic antifungal agent...MONISTAT i.v. (miconazole).

________________________ M.D.

Address________________________

City____________State____________Zip________

Specialty________________________

October 1978

Accept no substitute for your professional judgment

As a physician, you have the right to prescribe the drug which you believe will most benefit your patients. Now, substitution laws make it more difficult to exercise that right. In many states, unless you specifically direct pharmacists to dispense your brand-name prescription as written, they may be required by law to substitute another drug for your brand-name prescription.

This means that the ultimate drug selection is no longer yours; its source is left to the pharmacist's discretion. You will have forfeited your right to prescribe as you see fit. Preserve your rights. Specify that you will accept no substitution.

When you accept no substitutes...

- You ensure that your patient receives exactly that product you have specified on your prescription
- You choose the quality of the product dispensed to your patient
- You can exercise the right to select a product based upon its proven therapeutic performance and to select a manufacturer that stands behind its brand name or generic product
- You can support the kinds of research programs that are vital to new drug discovery and development
- You can help sustain important physician, pharmacist and patient education services supported by innovative, research-oriented firms

For complete information on the drug substitution law effective in your state, please consult your local Pfizer Representative.

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Pfizer **PHARMACEUTICALS**

ArMA 88th Annual Meeting
April 25—29, 1979
Safari Resort, Scottsdale

NEW DIRECTIONS

Wednesday April 25

Board of Directors Meeting — 8 a.m.
House of Delegates Meeting 1st General Session — 10 a.m.
Reference Committee Meetings — 2 p.m.

Thursday April 26

"Physicians Families" - Special Program 2 p.m.
Annual Golf Tournament — 12 noon
Annual Tennis Tournament — I p.m.
5th Annual National Calliope Concert — 6 p.m.
Reception and Steak Fry — 7 p.m.

FRIDAY APRIL 27

House of Delegates 2nd General Session — 8 a.m.
Scientific Program begins — 2 p.m.
ArMPAC Reception and Banquet — 7 p.m.

Saturday April 28

Breakfast Panel — 7 a.m.
Scientific Program Resumes — 9 a.m.
President's Reception and Banquet — 7 p.m.

Sunday April 29

Breakfast Panel — 7 a.m.
Scientific Program Resumes — 9 a.m.
Meeting concludes — 12 noon

Tenuate® Ⓒ
(diethylpropion hydrochloride NF)

Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of mon amine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence*. Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy*: Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children*. Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular*: Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System*: Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal*: Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic*: Urticaria, rash, ecchymosis, erythema. *Endocrine*: Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System*: Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous*: A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

Direct Medical Inquiries to
MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215, U.S.A.

Licensor of Merrell®

References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon, R.H., and Leyland, H.M.: A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy, Jan. 20-21, 1977.

Merrell

8-3921 (Y587A)

Whether overweight is a complicating factor... or just uncomplicated overweight.

Tenuate® Dospan® ⓒⅣ

(diethylpropion hydrochloride NF)

75 mg. controlled-release tablets

A useful short-term adjunct in an indicated weight loss program.

Overweight patients in certain diagnostic categories often require strict obesity control. Diethylpropion hydrochloride has been reported useful in obese patients with hypertension, symptomatic cardiovascular disease, or diabetes. While it is not suggested that Tenuate in any way reduces these complications in the overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. (Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.)

In uncomplicated obesity.

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

Clinical effectiveness.

The anorexic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.[1] And the unique chemistry of Tenuate provides "...anorexic potency with minimal overt central nervous system or cardiovascular stimulation."[2] Compared with the amphetamines, diethylpropion has minimal potential for abuse.

Tenuate–it makes sense. And it's responsible medicine.

Merrell

For prescribing information see opposite page

The evidence of experience

Since October 1974 when Motrin® (ibuprofen) was introduced in the United States, it has been used by more than 6,000,000 patients with rheumatoid arthritis* or osteoarthritis. Rarely has an ethical pharmaceutical product been prescribed for so many patients in so short a time. In addition, more than 450 studies presenting new data related to Motrin have been published.

The 6,000,000 patients already treated with Motrin is an objective measure of physicians' confidence in the ability of Motrin to relieve the pain and inflammation associated with rheumatoid arthritis and osteoarthritis.

So it is not surprising that in this short period Motrin has become the most frequently prescribed alternative to aspirin. Motrin relieves joint pain and inflammation as effectively as indomethacin or aspirin, but causes significantly fewer CNS and milder GI reactions. However, gastrointestinal bleeding, sometimes severe, has been associated with Motrin, aspirin, indomethacin, and other nonsteroidal antiarthritic agents.

*The safety and effectiveness of Motrin have not been established in patients with Functional Class IV rheumatoid arthritis (incapacitated, largely or wholly bedridden, or confined to wheelchair; little or no self-care).

© 1978 The Upjohn Company

Motrin 400 mg TABLETS
ibuprofen, Upjohn

The confidence that comes from experience—
one more reason to prescribe Motrin.

Please turn page for a brief summary of prescribing information.

Upjohn The Upjohn Company, Kalamazoo, Michigan 49001

The confidence that comes from experience—
one more reason to prescribe

Motrin 400 mg TABLETS
ibuprofen, Upjohn

Indications and Usage: Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Contraindications: Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

Warnings: Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.
Drug interactions. *Aspirin* used concomitantly may decrease Motrin blood levels. *Coumarin:* Bleeding has been reported in patients taking Motrin and coumarin.
Pregnancy and nursing mothers: Motrin should not be taken during pregnancy or by nursing mothers.

Adverse Reactions

Incidence greater than 1%

Gastrointestinal: The most frequent type of adverse reaction occurring with Motrin (ibuprofen) is gastrointestinal (4% to 16%). This includes nausea*, epigastric pain*, heartburn*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness*, headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

Incidence: Unmarked 1% to 3%; *3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

Overdosage: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

Dosage and Administration: Suggested dosage is 300 or 400 mg t.i.d. or q.i.d. Do not exceed 2400 mg per day.

How Supplied

Motrin Tablets, 300 mg (white)	
Bottles of 60	NDC 0009-0733-01
Bottles of 500	NDC 0009-0733-02
Motrin Tablets, 400 mg (orange)	
Bottles of 60	NDC 0009-0750-01
Bottles of 500	NDC 0009-0750-02
Unit-dose package of 100	NDC 0009-0750-06
Unit of Use bottles of 120	NDC 0009-0750-26

Caution: Federal law prohibits dispensing without prescription.

NIM-3

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001

ALDOMET®
(METHYLDOPA | MSD)
TABLETS: 500 mg, 250 mg, and 125 mg

MSD
MERCK
SHARP&
DOHME

NEW DIRECTIONS

AUXILIARY TO THE ARIZONA MEDICAL ASSOCIATION
CREATIVE MOMENTS '79

INSTRUCTIONS:

1. Fill in Registration Form below and mail to:
   Mrs Morton Comess
   6565 North Forty Third Place
   Paradise Valley, Arizona 85253
2. Entries are limited to:
   Three per person .... Adults
   Two per person .... Youth (13 years through 17 years)
   Two per per person .... Child (12 years and under)
3. Deliver item or items ready for display, to the Safari Convention Center-Scottsdale, 9 a.m.—12 noon, Wednesday April 25, 1979
4. Items *must* be picked up between 2:30 p.m. and 3:30 p.m. on Friday, April 27,1979

REGISTRATION FORM:

I would like to enter the following items in the CREATIVE MOMENTS '79 to be held April 25—27, 1979 at the Scottsdale Safari Resort.

Describe in Detail	Exhibited Professionally	Kit	Own Design	Child	Youth	Adult

(One form per person please)

NAME____ PHONE____________________

ADDRESS____

____

For further information contact:
Mrs. Robert W. Brazie
7434 North Sixty Second Street
Paradise Valley, Arizona 85353
Phone: 991-3624

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"Joint Life is the insurance of the '70's"

Doctor, HBA Life's

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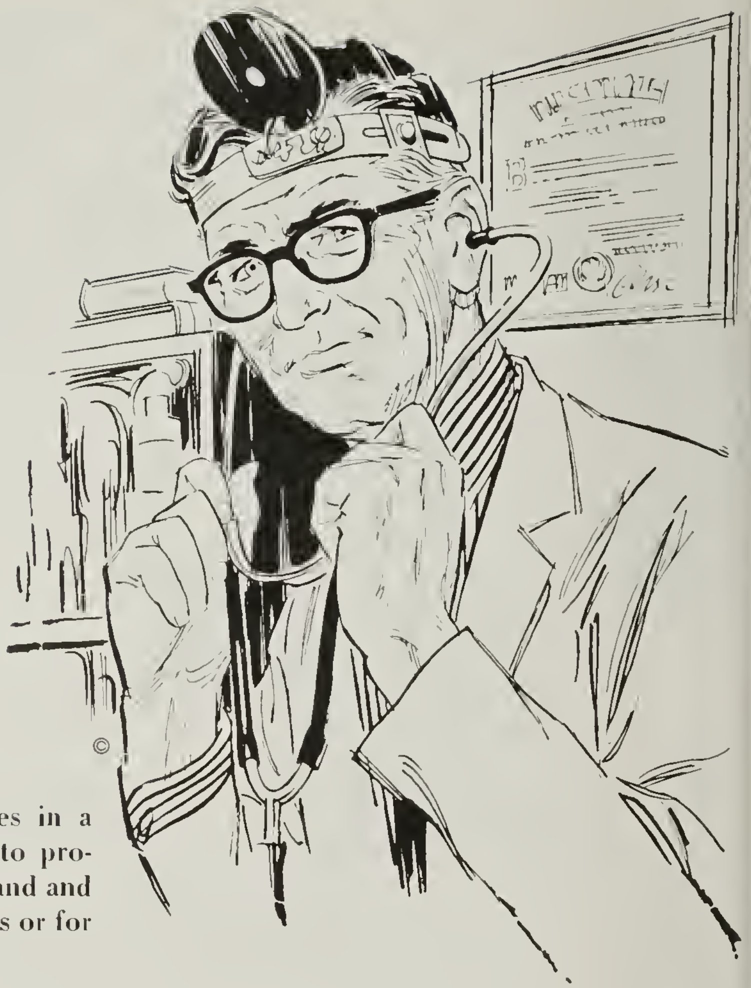
insures two people with only one policy, one low premium

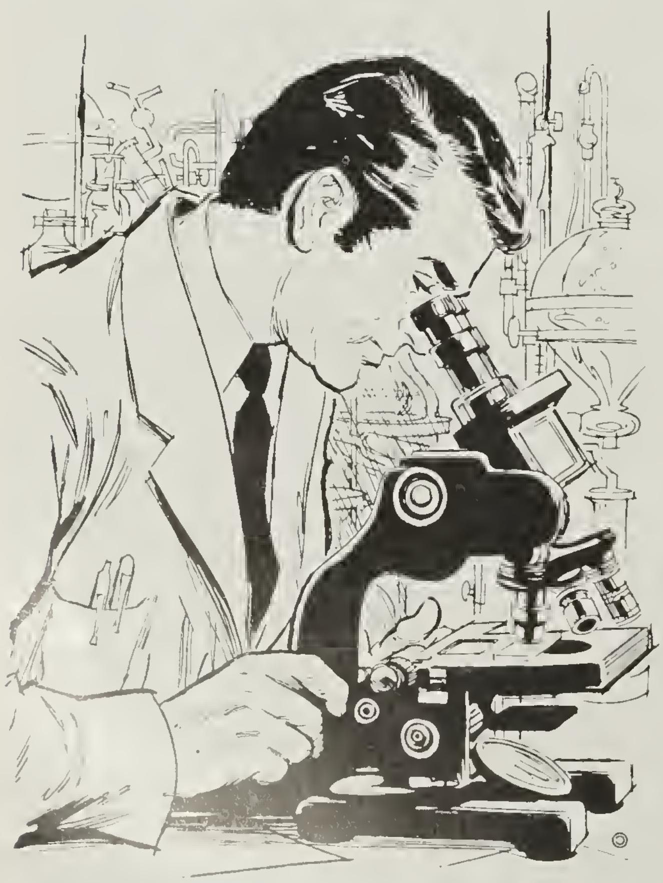
with these advantages:



BUSINESS INSURANCE: Two doctors, partners or associates in a professional corporation, will find this plan a low-cost way to provide funds if one of the two dies. It also may be used by husband and wife or father and son to provide funds to pay off special debts or for any of the other purposes for which life insurance may be used.

LOWER INSURANCE AGE: Often, one insured is somewhat younger than the other. The joint equal age can take years off the age of the older insured. The policy provides for the payment of the face amount upon the death of the first of the two insureds to die.

GUARANTEES SURVIVOR INSURABILITY: The surviving insured, within 90 days and prior to age 70, is guaranteed the right to purchase life insurance. If the surviving insured doesn't exercise this right and dies during this 90-day period, the conversion would automatically be made by the Company and the face amount, less the conversion premium, would be paid to his beneficiary.



DOUBLE FOR SIMULTANEOUS DEATH: If both insureds should die simultaneously, the sum insured upon their deaths would be paid to their beneficiaries.

CONVERTIBLE TO SINGLE LIFE: The Joint Life Insurance may also be converted to single insurance prior to the older insured's 60th birthday. The amount converted can be all on one life or the other or divided between the two as long as each does not take less than $1,000 of life insurance.

An HBA Life Agent would be glad to discuss it further at your convenience.

THE HBA LIFE
INSURANCE COMPANY
1337 N FIRST ST • PHOENIX • 258-4885

A Local Company Serving the West Since 1944

A reminder

ZYLOPRIM®

(allopurinol)

100 and 300 mg scored Tablets

- inhibits uric acid formation
- helps prevent urate crystal depositions in synovia
- reduces risk of uric acid lithiasis

INDICATIONS AND USE: This is not an innocuous drug and strict attention should be given to the indications for its use. Pending further investigation, its use in other hyperuricemic states is not indicated at this time.

Zyloprim® (allopurinol) is intended for:

1. treatment of gout, either primary, or secondary to the hyperuricemia associated with blood dyscrasias and their therapy;
2. treatment of primary or secondary uric acid nephropathy, with or without accompanying symptoms of gout;
3. treatment of patients with recurrent uric acid stone formation;
4. prophylactic treatment to prevent tissue urate deposition, renal calculi, or uric acid nephropathy in patients with leukemias, lymphomas and malignancies who are receiving cancer chemotherapy with its resultant elevating effect on serum uric acid levels.

CONTRAINDICATIONS: Use in children with the exception of those with hyperuricemia secondary to malignancy. The drug should not be employed in nursing mothers.

Patients who have developed a severe reaction to Zyloprim should not be restarted on the drug.

WARNINGS: ZYLOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR ANY SIGN OF ADVERSE REACTION. In some instances a skin rash may be followed by more severe hypersensitivity reactions such as exfoliative, urticarial and purpuric lesions as well as Stevens-Johnson syndrome (erythema multiforme) and very rarely a generalized vasculitis which may lead to irreversible hepatotoxicity and death.

A few cases of reversible clinical hepatotoxicity have been noted and in some patients asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. Accordingly, periodic liver function tests should be performed during the early stages of therapy particularly in patients with pre-existing liver disease

Patients should be alerted to the need for due precautions when engaging in activities where alertness is mandatory.

Nevertheless, iron salts should not be given simultaneously with Zyloprim. This drug should not be administered to immediate relatives of patients with idiopathic hemochromatosis.

In patients receiving Purinethol® (mercaptopurine) or Imuran® (azathioprine), the concomitant administration of 300-600 mg of Zyloprim per day will require a reduction in dose to approximately one-third to one-fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of Purinethol or Imuran should be made on the basis of therapeutic response and any toxic effects.

Usage in Pregnancy and Women of Childbearing Age. Zyloprim® (allopurinol) should be used in pregnant women or women of childbearing age only if the potential benefits to the patient are weighed against the possible risk to the fetus.

PRECAUTIONS: Some investigators have reported an increase in acute attacks of gout during the early stages of allopurinol administration, even when normal or subnormal serum uric acid levels have been attained.

It has been reported that allopurinol prolongs the half-life of the anticoagulant, dicumarol. This interaction should be kept in mind when allopurinol is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

A fluid intake sufficient to yield a daily urinary output of at least 2 liters and the maintenance of a neutral or, preferably, slightly alkaline urine are desirable to (1) avoid the theoretic possibility of formation of xanthine calculi under the influence of Zyloprim therapy and (2) help prevent renal precipitation of urates in patients receiving concomitant uricosuric agents.

Patients with impaired renal function require less drug and should be carefully observed during the early stages of Zyloprim administration and the drug withdrawn if increased abnormalities in renal function appear.

In patients with severely impaired renal function, or decreased urate clearance, the half-life of oxipurinol in the plasma is greatly prolonged. Therefore, a dose of 100 mg per day or 300 mg twice a week, or perhaps less, may be sufficient to maintain adequate xanthine oxidase inhibition to reduce serum urate levels. Such patients should be treated with the lowest effective dose, in order to minimize side effects.

Mild reticulocytosis has appeared in some patients.

As with all new agents, periodic determination of liver and kidney function and complete blood counts should be performed especially during the first few months of therapy

ADVERSE REACTIONS:

Dermatologic. Because in some instances skin rash has been followed by severe hypersensitivity reactions, it is recommended that therapy be discontinued at the first sign of rash or other adverse reaction (see WARNINGS). Skin rash, usually maculopapular, is the adverse reaction most commonly reported.
Exfoliative, urticarial and purpuric lesions, Stevens-Johnson syndrome (erythema multiforme) and toxic epidermal necrolysis have also been reported.
A few cases of alopecia with and without accompanying dermatitis have been reported.
In some patients with a rash, restarting Zyloprim (allopurinol) therapy at lower doses has been accomplished without untoward incident.

Gastrointestinal: Nausea, vomiting, diarrhea, and intermittent abdominal pain have been reported.

Vascular. There have been rare instances of a generalized hypersensitivity vasculitis or necrotizing angiitis which have led to irreversible hepatotoxicity and death.

Hematopoietic. Agranulocytosis, anemia, aplastic anemia, bone marrow depression, leukopenia, pancytopenia and thrombocytopenia have been reported in patients, most of whom received concomitant drugs with potential for causing these reactions. Zyloprim® (allopurinol) has been neither implicated nor excluded as a cause of these reactions.

Neurologic: There have been a few reports of peripheral neuritis occurring while patients were taking Zyloprim. Drowsiness has also been reported in a few patients.

Ophthalmic. There have been a few reports of cataracts found in patients receiving Zyloprim. It is not known if the cataracts predated the Zyloprim therapy. "Toxic" cataracts were reported in one patient who also received an anti-inflammatory agent; again, the time of onset is unknown In a group of patients followed by Gutman and Yü for up to five years on Zyloprim therapy, no evidence of ophthalmologic effect attributable to Zyloprim was reported.

Drug Idiosyncrasy: Symptoms suggestive of drug idiosyncrasy have been reported in a few patients. This was characterized by fever, chills, leukopenia or leukocytosis, eosinophilia, arthralgias, skin rash, pruritus, nausea and vomiting

OVERDOSAGE: Massive overdosing, or acute poisoning, by Zyloprim has not been reported.

HOW SUPPLIED: 100 mg (white) scored tablets, bottles of 100 and 1000; 300 mg (peach) scored tablets, bottles of 30, 100 and 500. Unit dose packs for each strength also available.

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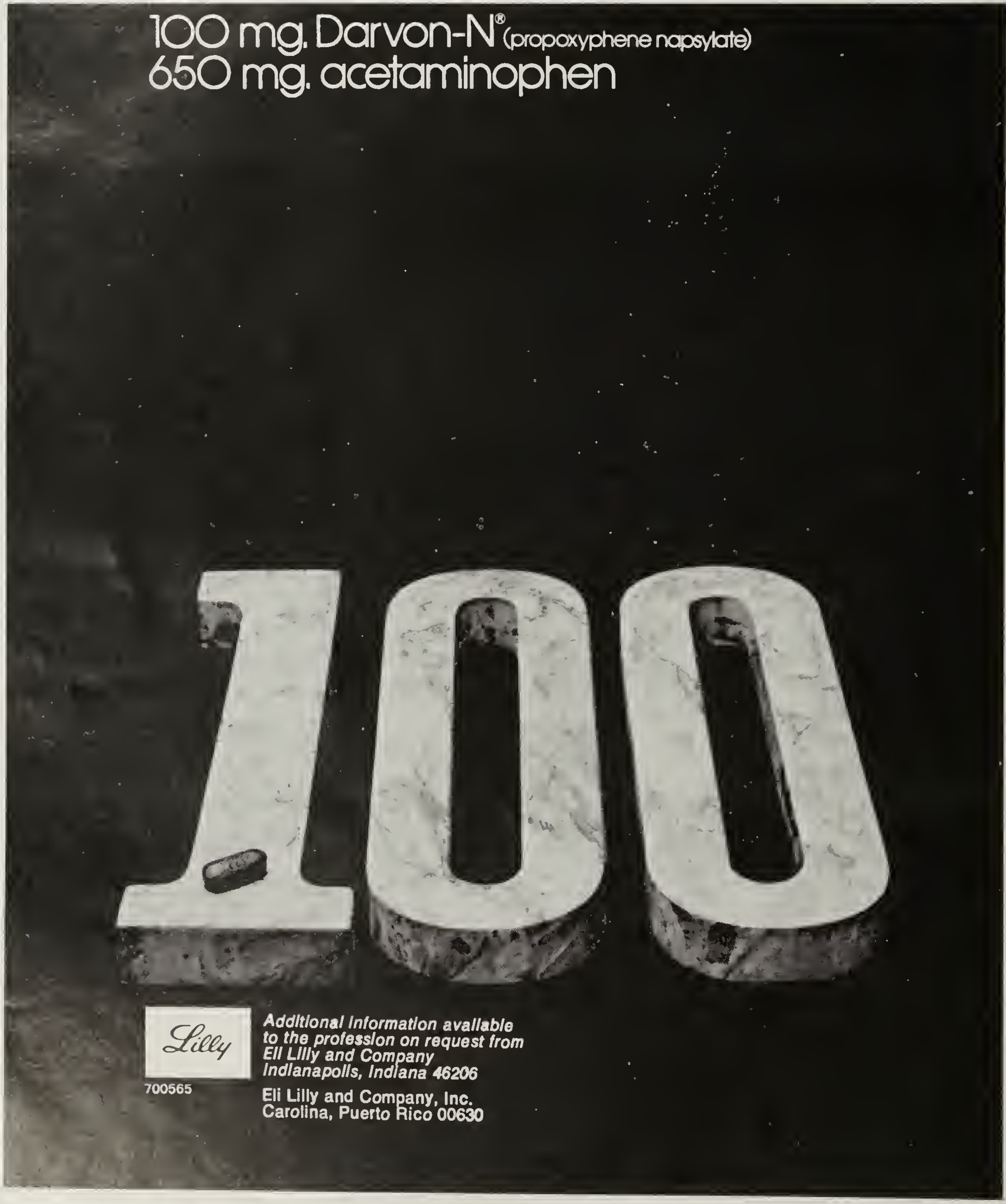

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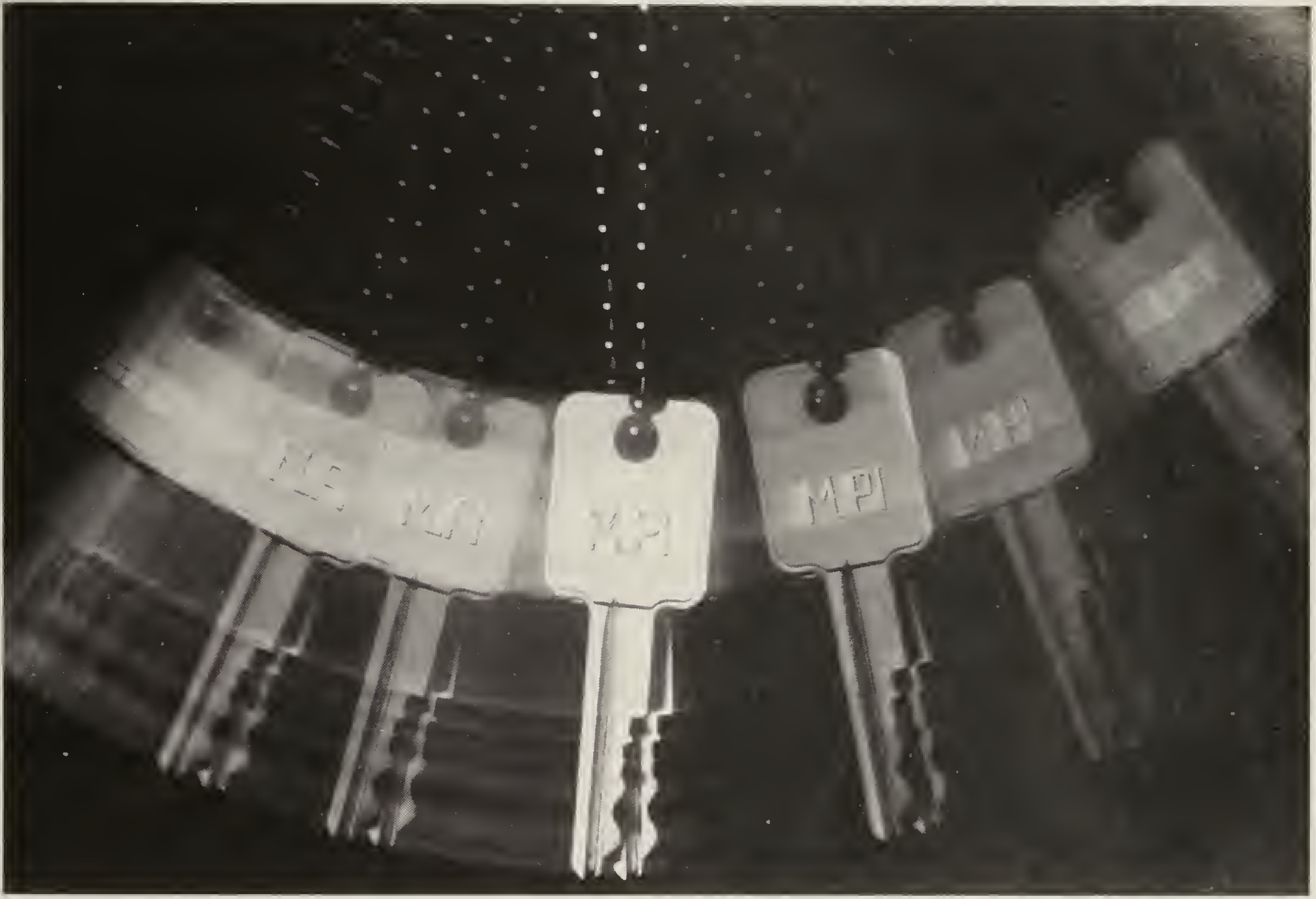

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Seminars in Chest Medicine

The Other Pink Puffers or Ventilation during Exercise

Thomas C. Rotkis, M.D.

The healthy person has an almost unlimited vetilatory capacity which can range from about 6 liters per minute at rest to between 150-170 liters per minute with severe exercise. Even at this level of ventilation it appears that other physiologic factors intervene before the limits of ventilatory reserve are exhausted. With such a wide range of function it is evident that there must be tight control of ventilation. Under resting conditions, ventilation is regulated primarily by centrally located chemoreceptors. During exercise the peripheral chemoreceptors become increasingly important. Despite the complexity of maintaining control over such a diverse system, normoxia is maintained and, except in the most severe exercise, acid-base status and arterial carbon dioxide (p_aCO_2) remain at resting levels. The intricate interactions by which this fine control is exacted are not fully understood.

Chemical Drives to Ventilation

The changes in ventilation during exercise are primarily modulated via the peripheral chemoreceptors. There is some information suggesting a multiplicity of receptors perhaps even on the tissue level; however, the only proven sites are the centrally located carotid bodies. There are three chemical variables that provide the primary stimuli for ventilation: the arterial hydrogen ion concentration (pH), the arterial oxygen pressure (p_aO_2), and the arterial carbon dioxide pressure (p_aCO). These three chemical variables are not equal in their ability to alter ventilation. Except at high altitudes or in people who have certain disease, pO_2 rarely varies. Moreover, the carotid bodies are sensitive to the level of arterial oxygen saturation and not to the absolute p_aO_2[7]. Since arterial blood is almost completely saturated until the p_aO_2 drops below 60 torr, it becomes clear that this is rarely an important factor in ventilation. Additionally, at levels below 60 torr the hypoxically induced hyperventilation lowers the p CO2 which then attenuates the hypoxemic effect by exerting an opposing influence. Since the blood brain barrier is impermeable to hydrogen ions, acute pH charges are relatively unimportant as an immediate factor in respiratory control. That leaves pCO2 as the primary determinant of ventilation. This is supported by the fact that there is an almost linear relationship between increase in ventilation and increase in CO2 production ($\dot{V}_{CO_2}$) with exercise.[14] At the extremes of exercise this relationship no longer holds; however, ventilation tracks changes in V_{CO_2} more closely than it does changes in oxygen uptake (V_{O_2}).

Steady State Work-load

In normal people, at a moderate level of aerobic work, exercise is characterized as being an isocapnic, isohydric, hypermetabolic state, and this condition is maintained despite as much as a 20-fold increase in VO and V_{co2}. The ventilatory pattern of someone going from rest to a steady state level of aerobic exercise can be divided into three phases: the immediate increase coincident with the initiation of exercise, a slower transient phase, and then the steady state level.[14] Although there is a reproducible pattern for each individual, a wide variation is found within the normal population.

Both tidal volume and respiratory rate increase with the first repiratory cycle following the initiation of exercise. The immediacy of this response has been taken as evidence that only neural input would be fast enough to regulate this phase. It is felt that these could be either proprioceptive signals from the exercising muscles and limbs or a sort of "spillover" activation of respiratory centers by the increased efferent signals generated by the cortical motor strip. Another mechanism has been postulated by Whipp and Wasserman.[20] They found that artifically stimulating cardiac output in dogs increased ventilation even when the carotid bodies were removed. Therefore, they believe that there may be a cardiodynamic component to Phase I.

As minute ventilation (V_E) increases, most of the demands are met by increases in the tidal volume until this reaches about one half of the vital capacity.[8] Beyond that point respiratory rate increases to provide the additional needs. Physiologically this makes sense since this pattern minimizes dead space ventilation.

Although phase II is slower than the initial phase, as long as the work load is below the anaerobic threshold,

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From: Division of Respiratory Sciences and Exercise and Sport Sciences Laboratory, U of A Tucson, Arizona. Dr. Rotkis, Fellow in Pulmonary Medicine.

he transient is complete within 45 seconds irregardless f the work load applied.[14] There is somewhat of a onsensus that this phase is humorally controlled. This as been demonstrated by Casaburi using sinusoidally arying work rates.[5] When minute ventilation was nonitored, it was found to be in phase with the CO2 lelivered to the lungs and out of phase with either the vork rate or the tissue level of CO2. The linking of entilation to CO_2 production is probably mediated hrough the carotid bodies, since resection of these rgans results in a slowing of phase II and a subsequent levelopment of a mild respiratory acidosis prior to btaining a steady state level.

It seems that Phase III also is determined by humoral actors. This again is seen with application of a varying vork rate.[5] If ventilation were tied to neural input from he exercising limbs, then peak work rate, which is out of hase with the peak level of end tidal CO2, would result n a fall in pCO2, and this situation is not observed. This s felt to be mediated through the carotid body hemoreceptors.

Our current understanding suggests that application f a fixed, aerobic work-load leads to a three stage response in ventilation, which is brought about by both humoral and neurologic stimuli. Of all of the factors which influence respiration the V_{CO_2} seems to be the most intimately tied to ventilation.

Increasing Work-Load

The ventilatory response to incrementally increased work extends many of the concepts seen with steady-state work. With exercise V_E, V_{O_2} and V_{CO_2} increase linearly until the subject reaches a level approximatey 60 % of his maximum work capactiy. Above this level while $\dot{V}_{O_2}$ continues to increase linearly with the increasing workload, both V_E and V_{CO_2} increases curvilinearly. This supports the concept of a tight linkage between V_E and V_{CO_2}. The point at which the inflection occurs has been termed the anaerobic threshold and is the point at which levels of lactic acid begin to increase in the blood. As the levels increase they are buffered initially by the bicarbonate system.

H^+lactate + $HCO_3 \rightarrow H_2O + CO_2$ + Lactate

The additional CO_2 production increases the stimulus to the carotid bodies, and the effect is augmented by the dropping pH as the bicarbonate ions are consumed. The ensuing hyperventilation creates a respiratory alkalosis that partially compensates for the metabolic acidosis and also increases the partical pressure of the alveolar oxygen, Even though the alveolar oxygen levels increase the arterial levels do not, and consequently the A-a O_2 gradient is widened with severe exercise.

Role of Peripheral Chemoreceptors

There is a wide range of normal values in healthy people in response to both hypercapnea and hypoxia. However, when an attenuated response to one condition occurs there is usually a dampened response to the other condition as well.[4] Since both stimuli are felt to operate through the carotid bodies, this suggests that there is either an impairment in the response of these organs to stimuli or that the central nervous system somehow alters the processing of afferent information from the carotid bodies. Of futher interest is that this situation is more characteristic of certain groups: high altitude natives, the blue bloater type of chronic lung patient, patients with cyanotic congenital heart disease, and the successful · endurance athlete. This has raised the question as to whether the insensitivity is genetic or environmentally induced. There is good evidence for an environmental influence. High altitude natives show a dramatic insensitivity to hypoxia when compared to residents of sea level. However, it has been found that when sea level natives spend prolonged periods at altitude, their hypoxic response becomes progressively blunted until after 15 to 20 years their response more closely approximates that of the high altitude native than that of the sea level native. On the other hand, if the high altitude native moves to the lowlands as an adult, he never loses his reduced hypoxic drive.

The increasing interest in athletics has brought this group under close study. Rebuck and Read were able to demonstrate decresed hypercapneic and hypoxic drives in successful endurance athletes, while sprinters fell within the normal range.[10] It is not entirely clear what sort of advantage this might provide unless it decreases the dyspnea that is associated with the hyperpnea of prolonged exercise.

Other data suggest that chemoreceptor insensitivity is a genetically determined trait. The Enga natives of New Guinea, a relatively uniform population, have found to have a significantly lower response to elevated CO_2 than Caucasians. Scoggins investigated five male elite distance runners, their parents, and six siblings, and compared these to a sedentary control group.[12] As has been demonstrated previously, the athletes had a markedly lower ventilatory response to hypoxia than did the controls; however, the sedentary family members had equally low values, and a least one parent in each family demonstrated this characteristic. Another study found a decreased hypercapneic response in trained swimmers and their families,[11] while hypercapneic insensitivity is seen in family memers of patients with chronic lung disese who retain CO_2. These studies strongly support the concept of genetic determination of this trait.

The available information suggests that the predominant determinant of chemoreceptor sensitivity is genetic; however, if a severe environmental stress is placed on the system, such as the chronic hypoxia of high altitude or cyanotic congenital heart disease, then the inherited pattern can be modified. The studies on athletes affirm the concept that decreased chemoreceptor sensitivity is a characteristic of successful endurance athletes; yet, they do not allow a staisfactory decision on whether people are born marathoners or train themselves to that point. It is ironic that a genetic trait which may be a factor in allowing one to meet the demands of a severe respiratory challenge, also may be a crucial component in shaping the pattern of respiratory failure that develops in the chronic bronchitic.

It is evident that ventilation is linked closely to the level of exercise. From current studies it appears that the principle driving force for this system is VCO_2 with its effect mediated through the carotid bodies.

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Seminars in Gastroenterology and Liver Disease

Alcohol and the Liver

Stephen Glouberman, M.D.

Editors:
Leon Rigberg, M.D.
Stephen Glouberman, M.D.
George Burdick, M.D.

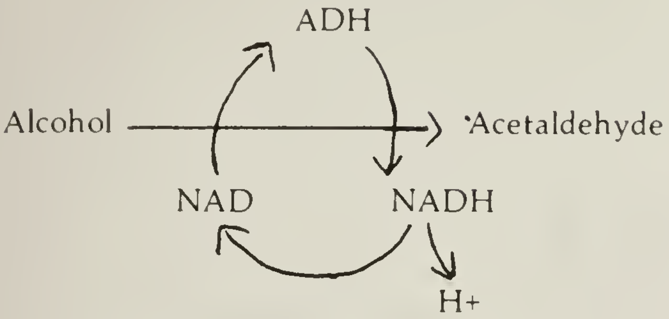
The consumption of alcohol is commonplace and widespread. Although it is socially acceptable to "bend one's elbow" at mealtime or at a social event, overuse of alcohol may lead to dire consequences. This brief review will discuss the metabolism of alcohol and then discuss the major disease states of the liver associated with alcohol intake.

Metabolism

Over 90% of ingested alcohol is abosorbed through the gastric and small intestinal mucosa, and then passes to the liver via the portal vein. A small percentage of alcohol is excreted through the lungs and by the kidneys.

From: 3411 N. 5th Ave., Phoenix, AZ 85013

In the liver, alcohol is oxidized to acetaldehyde by alcohol dehydrogenase (ADH):



Acetaldehyde is further oxidized in the mitochondrion to acetate and acetate is then available for use in many other reactions. Nicotinamide adenine dinucleotide (NAD) accepts a hydrogen ion from alcohol and this is then utilized in a number of different reactions. It is involved in the synthesis of fatty acids in the liver, which may accumulate and help to produce the fatty liver usually associated with alcoholic intake. Some of the newly formed acids and triglycerides are found in the peripheral blood resulting in hyperlipemia. Some of the fatty acids are metabolized in the mitochondrion with production of ketones and systemic ketosis ensues.

A further effect of this H+ ion is to shift the pyruvate-lactate equilibrium in the direction of lactate. Hyperlactacidemia may result. This will further result in hyperuricemia, as lactic acid inhibits uric acid secretion by the kidney. The shift of pyruvate towards lactate may also result in diminished gluconeogenesis, the so-called "alcholic hypoglycemia."

In addition to ADH, alcohol metabolism is enhanced by the microsomal ethanol oxidizing system (MEOS) and catalase. The MEOS is the second most important system involved in alcohol metabolism. It appears to come into play when the amount of alcohol is excessive for the amount of ADH available. It is thought that the non-ADH pathways play a role in the tolerance seen in alcoholics who are chronic and heavy imbibers. Furthermore, the MEOS system enhances the metabolism of many other drugs, resulting in higher doses of other medications being needed to produce their usual effects.[1]

Histologically, alcohol results in the production of mitochondrial changes in the liver with swelling of these structures. Often they reach large sizes sufficient to become evident as eosinophilic inclusions on light microscopy.[2] The cristae become abnormal. There is a proliferation of membranes of the smooth endoplasmic reticulum, with a resultant increase of microsomal enzymes. A decrease in cytoplasmic microtubules is seen by electron microscopy.[1]

Fatty Liver

Fatty metamorphosis is the most common hepatic condition associated with alcohol usage. This may occur after as short a time as two days, and maintaining a high caloric, high protein diet does not prevent its development.[3] The liver is usually enlarged, may be tender, and a mildly elevated transaminase may be seen. Often, however, there are no signs or symptoms.

There may be a threshold value below which alcohol will not produce a fatty liver. If 20% or less of the total calories ingested come from alcohol, a fatty liver may not develop. Each gram of alcohol metabolized produces 7.1 calories, and ½ liter of 86 proof whisky or 10 pints of beer contain about 170 gm. of alcohol, which is metabolized resulting in about 1200 calories. Reducing the concomitantly ingested dietary fat does not prevent the formation of the fatty liver,[4] if the volume of alcohol consumed is sufficient.

Several mechanisms have been proposed for the formation of the fatty liver. These include triglyceride synthesis, increased fatty acid production, increased fatty acid load, decreased triglyceride release, decreased fatty acid oxidation and diminished lipoprotein synthesis. Serum hyperlipemia is seen with fatty liver so that decreased triglyceride relase and impaired lipoprotein synthesis does not appear to play a role in man. The major component of the fat in the liver is dietary, so that if the individual is eating while drinking alcohol, this may be the major source of the fat. Decreasing the amount of fat in the diet will result in a lessened amount of fat in the liver, but will not completely prevent its development.

Although fatty liver is every common in alcohol overindulgence, and is frequently seen in alcoholic hepatitis and cirrhosis, most investigators do not believe that fatty liver directly results in the latter two conditions.

Alcoholic Hepatits

This condition is characterized by necrosis and inflammation, with polymorphonuclear leukocytes being very evident. It usually begins around the central vein, and may be more severe than the routine liver function tests would suggest. Clinically the major symptoms are anorexia, nausea, vomiting, abdominal pain and weight loss, although none of these need be present. The major physical findings include hepatomegaly, malnutrition, jaundice, ascites and fever. In approximately half of the patients with fever, no infection is found.[5]

Abnormal laboratory findings include anemia, elevated or lowered white blood cell counts, hyperbilirubinemia and hypoalbuminemia. The SGOT is almost always elevated to a greater extent than the SGPT, but rarely exceeds 300 units. The prothrombin time is a key prognostic sign with a 42% mortality being associated when this test is elevated.[6]

In addition to the histologic findings listed above, the presence of the Mallory body or alcoholic hyaline is considered the hallmark of alcoholic hepatitis. This is an eosinophilic accumulation of proteinaceous material, usually perinuclear in location and visible under light microscopy, which tends to appear in more severe cases of alcoholic hepatits. However, it is not pathognomonic for alcoholic hepatitis. Although usually being found in more severe instances of alcoholic hepatitis, its presence may not affect the survival in this condition.[6] Alcoholic hepatitis has been found in individuals following as little as three months of drinking to as much as thirty-[illegible] years. In one series, biopsy proven alcoholic hepatitis was found in 7.7% who drank less than [illegible] year.[5] The amount consumed is important, as it rarely develops if less than 80 gm. of alcohol is consumed per day, (8oz. 86 proof whiskey or 1 liter of wine).[6] The mortality of an individual episode is 4%, and the overall 5 year survival is 63%.[7] If the individual stops drinking, the 5 year survial is 80%.[6]

If alcohol consumption is stopped, at least 20%, and as many as 80% will go on to develop cirrhosis. It has been proposed that immunologic events are important in this regard. T lymphocytes have been found to be cytotoxic for liver cells in patients with alcoholic hepatitis, and this may perpetuate the liver disease and result in cirrhosis.[8]

Cirrhosis

A review of the clinical features of cirrhosis will not be undertaken here. The complications of cirrhosis, namely ascites, portal hypertension, and hepatic encephalopathy, are well known. The five year survival in patients with biopsy proven cirrhosis who stop drinking is 63%, 40% if alcohol consumption continues. It is 52% if ascites is present and drinking stops, and 33% if it does not. The corresponding 5 year survival rates if jaundice is present is 58%, and 33% and if hematemesis is present it is 35% and 21%.[9] If no ascites, jaundice or hematemesis is initially present, the 5 year survival is 89% if there is no further drinking, 68% if there is.

It is estimated that about 30% of alcoholics develop cirrhosis. If consumption of 160gm. of alcohol per day (slightly more than a pint of 86 proof whiskey) for 15 years will result in cirrhosis in 75%[1], then why does cirrhosis occur with less than the expected frequency? The answer is not known, but intermittent consumption, genetic susceptibility and the induction of the MEOS to metabolize more alcohol may all be involved.

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Nutrition for the Pregnant Diabetic Patient

Helen Cacheris, P.D.

Nutritionist

Donald J. Ziehm, M.D., Editor

The fundamental cornerstone in the management of diabetes is dietary planning and control. This factor becomes even more important in the management of the pregnant diabetic. At all times throughout the pregnancy the welfare of the fetus must be paramount.

Since the concepts of management of both diabetes[1] and pregnancy[2] have been reevaluated and changed during the past few years it is important that health professionals continue to be aware of the current principles and recommendations.

In diabetes the principles of dietary management are based on the concept of balance. Energy input (as measured by calories) is balanced with energy needs to achieve and maintain ideal weight. During pregnancy, total energy requirements are governed by the demands of maternal-fetal growth and overall increased metabolic needs. The adequately nourished woman whose diet is increased to support a growing fetus and

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From: Maricopa County Health Department, Dept. of Maternal and Infant Care, 1825 E. Roosevelt, Phoenix, AZ.

placenta will gain weight.[3] Any indicated weight reduction should never be undertaken during a pregnancy. Ketone bodies which form upon breakdown of body fat can be transported across the placenta and cause neurologic damage to the fetus. The American College of Obstetricians and Gynecologists recommends a weight gain of 24 - 30 pounds during normal pregnancy. A daily caloric intake of approximately 15% above non-pregnant requirements (an additional 300 calories or a total of 2400 calories per day)is recommended to accomplish this weight gain.

Based on these recommendations for the normal pregnant woman, the pregnant diabetic will require 2000 to 2400 calories or approximately 30-35 calories/kg of actual body weight to support the needs of pregnancy.[4] Calories should be increased if acidosis occurs.

The simplest method of evaluating caloric intake in pregnancy is to observe the pattern of weight gain. This normally consists of a minimal gain of 2 - 4 pounds in the first trimester, followed by a relatively linear rate of of gain averaging about one pound per week throughout the last two trimesters. The pattern and quality of gain is more important than the total amount. A standard prenatal weight grid showing the recommended pattern of weight gain compared with the patient's actual increase can serve as a teaching tool in conselling the patient.

Protein needs are increased in pregnancy to provide for fetal needs and to permit the required maternal physiologic adjustments of expansion of blood volume and growth of breast and uterine tissues. The most recent estimate of protein requirements in normal pregnancy suggest that an additional 30 grams per day is needed - 1.3 gram/kg for the mature woman and 1.5 gram/kg for the adolescent. Optimum protein intake is also important in control of diabetes. The diet of the pregnant diabetic should contain approximately 2 grams of protein per kg. of body weight per day, or about 100 to 120 grams per day, approximately 20% of the total calories. In metabolism the demand for energy takes first priority, so an adequate caloric intake is essential for optimum protein utilization.

During pregnancy adequate carbohydrate intake is important to meet the needs for diabetes control, as well as to meet fetal demands for glucose - approximately 45% of the total calories or a minimum of 200 grams of carbohydrate. This should be in the form of complex carbohydrates that are digested and absorbed slowly (starches, vegetables and fruits.)

The requirement for fat in the diet of the pregnant diabetic is not primary so the amount should be kept at moderate levels. Of the total caloric need approximately 30 - 35% (about 60 - 80 grams) may be supplied by fat.

Based on the above principles a diet prescription for a pregnant dibetic weighing 150 pounds may be:[5]

Calories: 2200
Protein: 120 grams
Carbohydrate: 250 grams
Fat: 80 grams

In addition to the total caloric requirement the daily division of the food intake must be considered. This is increasingly important in those patients who are receiving exogenous long-acting insulin in addition to small doses of regular insulin. Under these circumstances the time of insulin administration and the timing of food ingestion should be correlated in such a way as to provide glucose levels that approximate those of the non-diabetic pregnant woman. Fasting blood sugars below 100 mg/dl and two-hour post prandial sugars below 150 mg/dl are recommended for optimal outcome of pregnancy. The meal pattern should be divided into six feedings: three meals and a mid-morning, mid-afternoon and bedtime snack. Each feeding should provide both protein and carbohydrate. The bedtime snack should include an additional 25 grams of carbohydrate to avoid morning ketosis and hypoglycemia.

During the first trimester of pregnancy the diabetic may frequently exhibit low blood sugars, possibly due to the nausea and vomiting of pregnancy, decreased food intake or the increased uptake of glucose by the developing fetus and placenta. If fasting extends beyond 12 hours, the maternal blood glucose may drop as low as 40 - 45 mg/100 ml. Decreased maternal blood glucose produces a decrease in the fasting insulin level, resulting in a "starvation ketosis". The distinguishing feature of "starvation ketosis" is the lack of hyperglycemia which is characteristic of diabetic ketoacidosis. Treatment consists of glucose solutions and food rather than supplemental insulin. The pregnant diabetic must be extremely cautious during the first trimester and try to eat frequent small meals to guard against these hypoglycemic reactions.

The progressive rise of the placental hormones in the second half of prenancy ceates an increased need for insulin. Dosage requirements may steadily increase to 70% to 100% above pre-pregnancy needs at delivery. As pregnancy progresses the pregnant diabetic may develop ketoacidosis much more easily. This is not only a hazard to the mother, but can be life threatening for the developing fetus and must be avoided or, if present, treated promptly.

With rare exception every pregnant woman should receive iron and folic acid supplements. The pregnant woman requires additional iron for the maternal blood volume increase of 50% during the course of pregnancy and to supply the iron needs of the fetus and placenta. Most women are unable to meet the gestation requirment for iron by diet and iron stores. It is therefore recommended that supplements be given in the form of simple soluble ferrous salts in the amount of 150 - 3000 mg/day.[6]

The folic acid requirement is double that of a non-pregnant woman.[7] Folates have widespread physiologic funciton and without adequate supply cell division cannot proceed normally. 400 - 800 micrograms/day is recommended. The presence of overt folate deficiency should be suspected among patients with inadequate prenatal care and severe anemia.

The requirement for other vitamins increases modestly during pregnancy and can generally be met through diet. However, it has become customary to routinely administer vitamin supplements to pregnant women.

The successful outcome of diabetic pregnancy requires early identification and weekly monitoring by the health care team of both overt and gestation diabetics. Actually, the gestational diabetic needs the same kind of dietary management and control of maternal blood glucose concentrations as the insulin-dependent patient throughout pregnancy.

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Oncology

Management of a "Lump in the Neck"

Stanley W. Coulthard, M.D.
Charles F. Koopmann, Jr., M.D.

Editor:
David Alberts, M.D.

A "lump in the neck" presents commonly as a diagnostic and therapeutic problem. This problem may be diagnosed incorrectly or with inappropriate techniques. An organized and direct approach to evaluation of a neck mass is necessary to give the patient the best medical care. The basis for the diagnosis and treatment is a directed history, physical examination, and diagnostic evaluation. The resulting information will allow a reasonable working differential diagnosis and therapeutic approach. As a differential diagnosis is formulated, the cause of the lump is classified as 1) inflammatory, 2) congenital, or 3) neoplastic. In this article we will emphasize the sequence of a diagnostic evaluation, the completeness of the head and neck history and examination, and proper timing of biopsy procedures.

Inflammatory Processes

Cervical lymph nodes are commonly involved with inflammatory processes including specific granulomas and bacterial infections. The nodes undergo an initial inflammatory response and many progress to abscess formation. The initial treatment of many patients with a

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From: U of A Health Sciences Center, Dept. of Surgery, Sect. of Otorhinolaryngology, Tucson, AZ 85724.

lump in the neck is directed toward an inflammatory process. If, after a complete history and physical examination, there is evidence for an infectious process, such patients should be treated with an antibiotic for varying periods of time and followed closely for response.

Congenital Lesions

Two common congenital problems which present as neck tumors are the *thyroglossal duct* and *branchial-cleft cysts.* These cysts may be present for long periods of time before medical attention is sought. They are frequently noted before mid-teen years. Both of these cysts can have superimposed infections which confuse the definitive diagnosis. Branchial-cleft cysts are identified along the anterior border of the sternocleidomastoid muscle in its upper or middle portion. The relationship of the branchial-cleft defect to the neck skin and pharynx is variable, but there may be an associated sinus tract leading to the skin or pharynx. Thyroglossal duct cysts are most commonly noted in the midline of the neck and are frequently related topographically to the hyoid bone. It is noted that the cyst moves on swallowing. The thyroglossal duct cyst can become infected and require incision and drainage prior to a definitive surgical excision. Dermoid cysts are also found in the neck region. These cysts are usually asymptomatic and do not change in size. The dermoid cysts will seldom become infected. Treatment is directed at removal for diagnostic and cosmetic purposes.

Neoplasms

Neoplasms may occur as primary lesions in the neck or as a metastasis from a primary site elsewhere. Seventy to 80% of all asymmetrical cervical lymph node enlargements in the adult are malignant neoplasms that have risen from the primary site in the head and neck region. Squamous cell carcinoma is the most common histologic type of metastatic tumor in the cervical nodes. The primary site for the squamous cell carcinoma metastatic to regional neck nodes is usually the mucous membrane surfaces of the upper aerodigestive system. Lymph node lesions caused by Hodgkin's disease and the lymphocytic and histiocytic lymphomas are less frequent in the neck than are metastatic neoplasms. Salivary gland neoplasms will often present in the upper neck in either the submandibular gland or the tail of the parotid gland. These neoplasms are frequently asymptomatic and noticed only by chance. Lipomas, fibromas, neuromas, and carotid body tumors are found in the neck and must be included in the differential diagnosis of a neck mass.

Evaluation

A complete history including the patient's age, work activities, and possible exposures to carcinogens and infectious diseases is important. After a complete history has been taken, the physical examination is directed toward the head and neck region, but it must also be general in terms of examining *all* body systems. The head and neck examination is done by direct and indirect methods. If lesions cannot be directly inspected, the palpating finger is frequently helpful. Palpation is particularly important in evaluating submucosal lesions in the oral cavity and neck masses. The examiner's fingers can grasp a mass and determine its size, consistency, and mobility. Hence, palpation will frequently give information which relates to the diagnosis and also prognosis.

Laboratory investigations are directed toward determining the patient's hematological and biochemical status. Patients with a neck tumor should have a chest x-ray exam during the initial evaluation. This allows early identification of any area suspicious for metastatic or infectious disease. Arteriography is used when the neck tumor is thought to be intimately associated with the carotid systems or when the tumor is thought to be extremely vascular.

When the diagnostic evaluation has progressed through the history, physical, and routine diagnostic laboratory evaluation with no definitive diagnoses apparent, a thyroid scan should be obtained. This is particularly important if the neck mass is considered to be a thyroglossal duct cyst.

Direct endoscopic procedures such as direct laryngoscopy, bronchoscopy, and esophagoscopy are used to identify the occult primary neoplasms or to delineate neoplasms detected on physical examination.

Biopsy

Even after completion of a thorough head and neck history, physical, and laboratory evaluation, the clinician may still not be able to render a diagnosis. A surgical exploration of the neck for biopsy or definitive treatment is then indicated. It is extremely important that this be done at the end of an exhaustive diagnostic study. The surgeon who proceeds with a neck exploration should be able to deal with any of the numerous problems that may be identified. He should be aware not only of the technical aspects of treating the tumor, but also of the best therapeutic measures available. Incisions in the neck should be well planned to accommodate further extension of the surgery if necessary.

Summary

Evaluation of a neck tumor must involve close scrutiny of not only the neck but also the regional and systemic aspects of the patient. A cervical lymph node enlargement is considered metastatic carcinoma from a primary neoplasm of the head and neck region until proven otherwise. A complete head and neck examination is performed, using both direct and indirect endoscopic techniques with headlight and mirror. A neck mass is biopsied only after an exhaustive history, physical examination, and laboratory evaluation fail to reveal a diagnosis. Finally, if the physician initiates a neck exploration, he should be able to cope with all the numerous possible neoplastic, inflammatory, and congenital problems he may encounter.

Psychiatric
Disorders

ONE'S OWN WORST ENEMY

William B. McGrath, M.D.

"Every man has his breaking point." The statement was made by Dr. Karl Menninger durng World War II. At the time he was asking for a compassionate attitude toward cases of combat fatigue

In peaceful, more ordinary times and roughly comparable circumstances, such a statement about psychiatric casualties can be unfair and misleading. The inference is that breakdowns occur in individuals who have proven somehow weaker than their fellows. This misconception adds shame to the other burdens of the patient and prolongs the prejudice of society against him.

Actually the stressors involved in psychophysiological disorders are seldom external. Pressures from one's environment permit the externalizing or projection of blame, so that the patient need not excuse or blame himself. Secondly, one can react to external stress: fight or escape or resign one's self. Thirdly, when the pressure is from the outside one can have hope, hope that changing conditions will bring relief.

It is the internal stressor which renders a person most vulnerable to neurotic or psychophysiological illness. Implied always is conflict. The conflict is intrapsychic, between opposing wishes or courses of action. And to be pathogenic, one of the drives has to have been kept out of consciousness. When alternatives are visible one can make a choice. Whatever the ideals or desires or motives that determine the decision, we should be reminded that the choice is usually not between right and wrong but rather the choice of a (seemingly) lesser evil.

Examples of common and most significant stressors will be mentioned.

A psychosomatic price will almost inevitably be paid for the rationalization that one has to be chronically dishonest with himself or others. Certain business practises came to mind. "How can we compete and make a profit without some cheating, some misrepresentation?" Alcoholism may be the most frequent disease-in-process relating to this conflict.

In personal relationships there are many varieties and degrees of deception which appear to be unavoidable (again, the lesser evil). A wife may pretend to herself that she goes along with being intimidated or domineered because she lacks direction or is ill-equipped to jeopardize her own and her children's security.

The husband of a passive-aggressive woman may convince himself that he needs no friends or recreations or common interests. He may be quite unaware that he

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From: Camelback Hospital, 5055 North 34th Street, Phoenix, AZ 85018. Dr. McGrath, Medical Director

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s crippling himself to prevent her from having lestructive custody of their children.

Another example is wishful thinking that devotion night extinguish any feeling of resentment in having to are for a loved one who has been or is becoming ncompetent.

People do not realize that there is no feeling or emotion which is, per se, good or bad. And people should e taught that emotions require outlet only into onsciousness and do not always need discharge in ction. Feelings, such as self-pity, do not accumulate by dwelling on them. What can accumulate is not the emotion but the habit of verbalizing it too tiresomely.

The loss of one's spouse in death or divorce is not so athogenic as the loss of one's most cherished identity (husband,wife). What hurts more than loss of a job is oss of one's title: executive, wage earner. Paradoxically, he worst stress of all is no stress; e.g., in the loss of dentity and dedication when retirement is ill planned or remature.

A very common and rather severe stress results when n individual persists in some pattern of behavior which s contrary to conscious judgement and avowed desire: smoking, drinking, philandering. Corollary is the nescapable psychophysiological consequence of living constantly in the risk of losing face; e.g., when practising gross fraud or having an affair.

In avoiding unhealthy stressors and in preventing psychophysiological disorders, people do need a return to some kind of religion, even if it is only handcrafted. To our dismay, a majority of patients have never even considered certain basic principles and values by which they intend to live. Every individual in early adult life should make up his mind about a few of the issues, primarily but not exclusively moral, which he is bound to encounter. The uncertainty of so-called situation ethics is harmful. Having neither clarity nor conviction about how he will act or what he will tolerate in any set of circumstances, a person becomes the chronic victim of circumstances. Unable to foresee conditions in which he might find or place himself, he will be indecisive and insecure. If he cannot have sterling trust in himself he cannot trust anyone else, and he will live in tense suspicion in all his dealings and relationships.

When a man has resolved in advance that there are no circumstances in which he will cheat on his wife or in his business, then he will not have to keep making day to day and shifting decisions about such fundamental concerns. When a man knows the limits of what he will tolerate, in the way of intimidation or humiliation or abuse, others will sense his integrity, respect him and not try to interfere with his work.

The vampires which ruin our health, in summary, are mostly within our own minds. They are the unconscious antagonists which bleed our identities and integrity and freedom of choice. They will not attack if we clearly define our private code of honor and if we know that we can be totally honest with ourselves in trying humanly to live up to it.

Arizona Perinatal Program Past, Present and Future

Part II

Harold D. Gabel, M.D.

Executive Director

This was the program's mission. It is being accomplished by the following.

1. *Facilitating development of interhospital agreements based on criteria for levels of patient care to develop a statewide regionalized system.*

"Recommendations and Guidelines for Perinatal Care Centers in Arizona" were developed by the Arizona Perinatal Program. This system defines the resources, manpower and service that must be provided at each hospital level of care; that is primary, secondary and tertiary (most sophisticated) care centers. The recommendations originally drafted in 1975 have been modified by experience and have been utilized to designate four Tertiary Care Centers and two Secondary Care Centers in Arizona. More hospital administrators and physicians are requesting this procedure for their institutions. The Arizona Perinatal Program stands ready to assist all hospitals in a self-evaluation process and to assist them to function at a level at which they are capable of performing. In addition, formal designation as a primary, secondary, or tertiary center can be provided by an Arizona Perinatal Program evaluation committee with its statewide representation.

From: 810 W. Bethany Home Rd.,
Phoenix, Az. 85014.

2. *Establishment of a consultation system of perinatal health providers all over Ariozna.*

Twenty-four hours a day, seven days a week, expert telephone consultation is available in Phoenix and Tucson. Any health provider in Arizona can call published numbers in Phoenix and Tucson and talk to a neonatologist or perinatologist about a particular problem, consultation may lead to the transport of the patient involved.

3. *Establishment of a transportation system for high-risk mothers.*

Arrangments have been made for ground and air transport for high-risk maternity patients from anywhere in Arizona to a tertiary level center in Phoenix or Tucson. These transports are paid for by Arizona Perinatal Program when no other source of payment is identified. The mode of transport is determined during the consulatation between health provider and tertiary center specialist. It is based on the clinical situation and the geographical location of the patient. One thousand two-hundred nineteen transports have been provided since the inception of the program and utilization is expected to increase this year. The primary reasons for transports are, in decreasing order of priority: premature labor, premature rupture of the membranes, pre-eclampsia and bleeding. This list comprises 95% of the indications for transport thus far. At this point, the makeup of the transport team dispatched from the medical center, the skills of transport personnel, as well as equipment required, is being studied.

4. *Development of a system of record keeping which permits adequate evaluation on the network's performance.*

An eight-part clinical record, which is computer capable, covering the entire perinatal period for both mother and infant has been developed. It is designed to be used by care providers and hospitals; it enables a continuous survey of mother and child for risk factors at any time in the perinatal period. Computer summary printouts on individual patients are available to involved health care providers. Statistical data is available to participating hospitals on a monthly basis. At present, approximately 50% of Arizona's births are recorded on this system. All information on computer is protected by strict patient confidentiality guidelines. Instruction manuals and a slide/tape presentation on the use of the record system has been developed. The use of the record system has been endorsed by the Arizona Medical Association Maternal and Child Health Care Committee and is available to any interested health provider or hospital in Arizona.

5. *Development of a health education program working in coordination with the entire regionalization effort.*

A Health Educator hired by Arizona Perinatal Program coordinates health education programs for professionals, patients, and the public in the area of perinatal health care. In the field of professional continuing education, each of 39 hospitals in Arizona has been surveyed to identify those professional groups and subject areas where continuing education is needed. Also identified is a liaison person in each of these institutions. Secondary centers and tertiary centers and the office of the Arizona Perinatal Program are providing much of this inservice continuing education to the indentified hospital groups, as well as, much of the continuing perinatal education presently being provided in Arizona. In 1977, 61 programs at 32 hospitals were presented. These were attended by 447 nurses, 86 doctors, and 10 other health professionals. More programs are planned for this year. Requests and suggestions are welcomed. The program also provides funds for long and short term training programs for nurses who are interested in developing their skills in perinatal health care.

In the area of public and patient education, perinatal education programs and workshops have been provided in several cities, counties and on the White Mountain Apache Reservation. Materials are currently being developed to help patients to identify high-risk factors in pregnancy and enable them to seek help early to deal with these problems in a therapeutic manner.

The Arizona Perinatal News is a newsletter published three times a year by the Arizona Perinatal Program. It is used to inform health care providers and other interested persons of what is currently happening in the area of perinatal health in Arizona.

6. *Payment for the transport of non-routine laboratory specimens.*

A manual has been prepared which describes tests which can be done to detect and monitor high-risk pregnancies and neonates. Specimens may be sent to St. Joseph's Hospital and Medical Center Regional Perinatal Laboratory in Phoenix, to have the tests performed. The transport of such specimens is paid for by the Arizona Perinatal Program when no other means of payment can be indentified.

To evaluate the efficiency of the Arizona Perinatal Program, several studies are underway.

One study will evaluate the cost-benefit efficiency of the regionalized perinatal approach. It is designed to examine the hypothesis that a regional program of perinatal health care with an emphasis on the care of high-risk maternity patients in conjunction with transport when necessary would be more cost effective than a program of transport and care of newborns only.

A newborn follow-up prospective study of 200 newborns, which attempts to identify neurologic abnormalities at several points up to five years of age after neonatal intensive care unit admission, is underway. This study seeks to determine if neurologic or psychologic abnormalities are present in these infants. If abnormalities are significant and a correlation with prenatal risk factors can be done, a contribution can be made.

In addition, a group from Johns Hopkins University is studying the eight regionalized area programs supported by the Robert Wood Johnson Foundation grants. A study will compare maternal and infant morbidity and mortality characteristics of each area population before and after regionalization began.

The perinatal consumer will also be given a chance to evaluate the perinatal care system from the perspective of their own birth experience. A questionnaire developed by the Arizona Perinatal Program Maternity Follow-up Task Force seeks to determine areas of satisfaction and dissatisfaction amoung high and low risk pregnant women, some of whom were transported to other cities to have their birth experience.

What is the future direction for this program?

-Continued close cooperation between all members of the practicing perinatal community is fundamentally important to the success of the program. These cordial relationships related to the regionalized program will be fostered and encouraged throughout the State of Arizona.

-An increasing effort will be made to designate additional primary and secondary care centers so that the network which already exists is made even more complete.

-The data system currently utilized will be expanded to include most of the births in Arizona. This will enable health care providers to utilize the data within the system to the mutual benefit of mothers and babies in present and future pregnancies. The computerized data information should be available for any and all research purposes within the guidelines of patient confidentiality. This system should allow physicians and hospitals to evaluate perinatal health care in their own areas as well as comparing their infomation with the rest of the State.

-The educational program, building upon previous experience, will develop educational packages in all topics of specialized perinatal care for use in hospitals where these skills are needed. In addition, regional meetings for perinatal health professionals will continue to be a priority. A public information campaign to create an awareness of the meaning of 'perinatal'', high-risk pregancies, and the urpose of the Arizona Perinatal Program will also begin. This will begin hrough the greater use of TV, radio and ewspapers. A speakers bureau, a booth t the State Fair, a perinatal'' call-in'' ervice for consumers, and a film library re envisioned.

-Programatic areas of future concern nclude the prenatal diagnosis of genetic isease, programs dealing with teenage pregnancies and programs which provide prenatal care for the indigent.

In closing, I would like to state that the success of the Arizona Perinatal Program will be demonstrated when all births in Arizona are achieved with a minimum of maternal and infant morbidity or mortality. Total success will mean that each patient will receive needed services whereever and whenever they are required. This result will be achieved with the least possible economic burden on both parent and hospital and with the most positive family birthing experience possible. The adherence to the principles of a regionalized health care system will bring such a result about.

If the system has provided successes thus far and if those who read this article agree, I strongly urge that you and your colleagues work toward the goals proposed by the program in all of your clinical and community activities.

State of the Art

Advances in the Management of Ovarian Cancer

David S. Alberts, M.D.

Epidemiology

Ovarian carcinoma is becoming an increasingly nportant epidemiological problem. There has been a wo-fold increase in the incidence of this disease during he last four decades and it has become the leading cause f death from gynecologic tumors. It is estimated that here will be 17,000 new cases of ovarian carcinoma in 978 and 10,800 deaths during this period.[1]

Cell Biology

Hamburger et al have studied the biological haracteristics of ovarian cancer stem cells grown *in itro*.[2] Cytogenetic studies on clonogenic cells from 5 atients showed hyperdiploidy in 4 with more than 60 hromosomes per cell. In addition, double minute hromosomes were seen in 2 patients and these have nly been observed in malignant tissues. The growth raction of these stem cells varied between 30 and 100% s documented by tritiated thymidine suicide studies. here also was evidence that macrophages were equired for optimal tumor stem cell proliferation. Vhen the phagocytic cells were removed using carbonyl on, tumor colony formation was markedly diminished n 3 study patients. Finally, exposure of ovarian tumor cells *in vitro* to the experimental anticancer drug cis-diamminedichloroplatinum (cis-platinum) resulted in a wide variation of colony inhibition from patient to patient. This suggested variability in drug sensitivity, at least to one anticancer drug to which none of the study patients had had previous exposure.

Staging and Histology

The FIGO staging system for ovarian carcinoma appears in Table 1.[3] Unfortunately, over 60% of patients present at the time of diagnosis with stages III and IV disease. The fact that the five year survival rate for patients with advanced disease (stages III and IV) has in the past not exceeded 10% accounts for the high death rate for this disease. Although the 5 years survival rate for patients with stage IA disease may exceed 90%, stage IB, IC and IA with extracystic excrescences or cyst rupture have survival only in the range of 60%.[4] Survival for stage II patients ranges between 40 and 60% at 5 years.

Tumors of epithelial type make up 85% of ovarian carcinomas. Of these tumors, serous cystadenocarcinoma accounts for over 50% of cases. The rest of the histologic types include mucinous cystadenocarcinoma, endometrioid carcinoma, clear cell carcinoma and undifferentiated carcinoma (Table 2). Of these, serous cystadenocarcinoma carries the worst prognosis. The majority of patients with serous cystadenocarcinoma

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rom: U of A Health Sciences Center, Sect. of Hematology and ncology, Tucson, AZ 85724

Table 1
FIGO (Federation International Gynecology and Obstetrics)
Staging Classification of Ovarian Cancer of Epithelial Type[3]

Stage	Definition
I	Growth limited to ovaries.
A	Growth limited to one ovary; no ascites. (i) No tumor on external surface; capsule intact. (ii) Tumor on external surface or capsule ruptured or both.
B.	Growth limited to both ovaries; no ascites. (i) No tumor on external surface; capsule intact. (ii) Tumor on external surface or capsule(s) ruptured or both.
C.	Tumor stage is IA or IB, plus ascites* or malignant cells in peritoneal washings.
II	Growth involving one or both ovaries, with pelvic extension.
A.	Extension or metastases or both to uterus or tubes or both.
B.	Extension to other pelvic tissues.
C.	Tumor stage IIA or IIB, plus ascites* or malignant cells in peritoneal washings.
III	Growth involving one or both ovaries, with intraperitoneal metastases outside the pelvis or positive retroperitoneal nodes or both. Tumor limited to true pelvis, with histologically proven malignant extension to small bowel or omentum.
IV	Growth involving one or both ovaries, with distant metastases. Pleural effusion must contain malignant cells to indicate stage IV disease. Parenchymal liver metastases indicate stage IV disease.
Special Category	Unexplored cases thought to be of ovarian carcinoma.

* Peritoneal effusion that, in the opinion of the surgeon, is pathologic or clearly exceeds normal amounts or both.

have advanced disease at the time of diagnosis, whereas mucinous cystadenocarcinoma and endometrioid carcinoma have higher proportions of patients with earlier stage disease.

The degree of anaplasia existing within the tumor[5] may be more important in determining prognosis than cell type. There appears to be a close relationship between survival and Broders' histological grades of malignancy.[6] Grade I histology includes 0 to 25% undifferentiated cells; grade II, 25 to 50% undifferentiated cells; grade III, 50 to 75% and grade IV, 75 to 100%. An example of the effect of histological grade on survival is the fact that patients with stage I, histological grade I serous cystadenocarcinoma have a five year survival rate of 90%.[5] However, those with grade II lesions have only about a 50% five year survival rate.

Table 2
Ovarian Cancer Cell Types

Type	Frequency
Serous cystadenocarcinoma	40%
Mucinous cystadenocarcinoma	12%
Endometrial Carcinoma	15%
Undifferentiated adenocarcinoma	15%
Clear cell carcinoma (mesonephroma)	6%
Granulosa-theca cell tumor	5%
Dysgerminoma	1%
Malignant teratoma	1%
Metastatic carcinoma	5%

Surgical and Nonsurgical Staging Procedures

Surgical Management. The thoroughness of exploratory laparotomy at the time of diagnosis has proven a major factor in determining prognosis for individual patients Lower abdominal incisions are not adequate for the staging of ovarian cancer. There must be adequate access for both observation and biopsy of upper, intraabdominal space lesions. In addition to a bilateral salpingo-oophorectomy, total abdominal hysterectomy and omentectomy, exploratory laparotomies should include evaluation for unilateral and bilateral ovarian disease, observation for peritoneal implants throughout the intraabdominal and pelvic space and cytological evaluation following intraabdominal washings. Disease should particularly be looked for on the undersurface of the diaphragm because there is a high incidence of occult disease in those areas. There is now evidence that agressive surgical debulking of tumor masses to less than 2 cm residual disease is likely to result in markedly improved five year survivals. Thus, attempts should be made during the initial exploratory laparotomy to both thoroughly observe the intraabdominal and pelvic spaces as well as to remove as much of the disease as is possible.

Non-Surgical Staging Procedures. There is an increasing interest in the use of peritoneoscopy for the non-surgical evaluation of upper abdominal disease in ovarian cancer patients. Rosenoff et al have shown with peritoneoscopy that almost 45% of patients with laparotomy-proven stage I or II disease have evidence of diaphragmatic metastases.[7] There was a 70% incidence of such metastases in patients with laparotomy-proven stage III or IV disease. Unfortunately, peritoneoscopy alone is not an adequate replacement for a thorough exploratory laparotomy because it does not allow evaluation of the entire intraabdominal and pelvic spaces.

Recently, we have compared computed axial tomography to ultrasonography in the evaluation of lower abdominal and pelvic masses in patients undergoing surgical evaluation of tumor mass size. Al 15 patients in this study had surgical exploration of their tumor within 1 month of CAT or ultrasound scanning The results of this study appear in Table 2. Of 12 patients who had surgically proven pelvic masses, 10 had true positive ultrasound and CAT scans. The ultrasound and CAT scans were complimentary so that in no patient were both scans falsely negative. We have concluded that ultrasound scanning of the lower abdomen and pelvis is an accurate, safe and relatively inexpensive technique for evaluating tumor size. It can be used for followup tumor evaluations in patients on therapy for this disease. On the other hand, CAT scanning can be a valuable technique when the baseline ultrasound scan is negative. It may also give finer anatomical detail of the tumor masses, especially those within the uterus.

Therapy

Radiation Therapy. Radiation therapy plays an uncertain role in the management of ovarian cancer. It requires 4000-5000 rads to sterilize microscopic aggregates of adenocarcinoma, 6000 rads to sterilize > 2 cm disease and 7000 rads to sterilize 2-4 cm disease. Because the kidneys cannot tolerate more than about 2500 rads and the liver not more than 3500 rads, radiation therapy should not be used, except for palliative purposes, for the treatment of advanced stage III and IV disease. Furthermore, the results of early studies have shown that pelvic irradiation following surgery does not improve survival or disease-free survival for patients with stage I, II or III cancer.[8,9]

Radiation therapy has been used successfully as adjuvant treatment for high risk recurrent stage I and II ovarian cancer. Dembo has reported the results of a randomized study of stage IB and II disease.[10] His group at the Princess Margaret Hospital in Toronto has studied pelvic irradiation alone versus pelvic irradiation followed by chlorambucil versus pelvic irradiation plus abdominal irradiation (moving strip technique). Survival at four years was 82% in the pelvic plus abdmoinal irradiation therapy group versus about 50% in the other two treatment groups. There have been no intraabdominal recurrences in the patients treated with whole abdominal plus pelvic irradiation as opposed to about 25% intraabdominal recurrences in the other two groups of patients. Unfortunately, this study did not compare chemotherapy alone to the radiation therapy treatments. The study does show that pelvic irradiation alone is not and adequate treatment for even localized disease.

Smith et al have carried out a study at the M.D. Anderson Hospital and Tumor Institute comparing melphalan alone to whole abdominal plus pelvic boost irradiation for stages I through III (minimal residual disease less than 2 cm) cancer.[11] Melphalan was given monthly for 12 cycles. The moving strip technique was used for the whole abdominal treatment. As of May 1974 there were 70 patients in the radiation therapy alone group and 79 in the melphalan group. Actuarial survival at five years was 71% in the radiation therapy patient group and 72% in the melphalan treated patients Forty five percent of those receiving radiation therapy and 63% of those on chemotherapy had no evidence of disease. While toxicity was relatively mild in the melphalan group, 7 of the 70 patients given radiation therapy required surgery because of an injury to the small intestine. On balance then, melphalan therapy appeared to be the better treatment in this study.

Table 3

Overall Efficacy of Scanning Procedures In Patients with Surgical Documentation of Tumor Status

	True Positives	True Neg's	False Neg's	False Positives
CAT Scan	10	3	2	0
Ultrasound	10	3	2	0
Combination CAT + Ultrasound	12	3	0	0

Chemotherapy. There are a large number of anticancer drugs possessing important activity against ovarian carcinoma.[12] Table 4 indentifies those drugs which appear to be most effective in inducing objective responses when used as single agents. Response rates vary from 16-50% and are relatively short lived for these drugs when used individually.[12]

There is now evidence that multiple agent chemotherapy is more efficacious than single agent treatment of advanced ovarian cancer. Young et al have recently reported that a combination of hexamethylmelamine-cyclophosphamide- methotrexate-5-fluorouracil (HEXACAF) as compared to melphalan resulted in a significantly higher overall objective response rate (75 vs. 54%), higher complete response rate (33 vs. 16%) and longer median survival duration (29 vs. 17 months).[9] There are several other ongoing, randomized trials of various drug combinations versus melphalan for advanced disease. In most of these studies melphalan has induced an objective partial plus complete response rate between 25 and 30% as compared to a 40-50% response rate for the two drug combinations.

Adriamycin-cyclophosphamide (A-C) therapy has been reported to induce response rates of 50-80%.[13,14,15] This great variability may possibly be explained by the use of differing response criteria and patient populations in these studies. As an example of the latter problem, Young et al have shown that higher response rates are associated with the presence of small residual disease as compared to extensive disease prior to the initiation of therapy.[9] There was an 84% response rate for patients with less than 2 cm residual disease as compared to a 53% response in those with more advanced lesions.

Erhlich et al have added cis-diamminedichloro platinum (cis-platinum) to A-C and have reported 61 to 76% partial plus complete responses depending upon the

Table 4
Single Agent Therapy in Ovarian Cancer*

Drug	Number of Patients	Response†
Melphalan	494	47%
Cyclophosphamide	126	49%
Adriamycin	33	36%
Hexamethylmelamine	53	41%
Cis-platinum	25	16%
Methotrexate	16	25%
5-Fluorouracil	81	32%

* Adapted from R. C. Young, Chemotherapy of Ovarian Cancer: Past and Present. Seminars in Oncology 2:267-276, 1975.

† Response criteria were variable and did not require 50% decrease in size of tumor masses.

schedule of the cis-platinum.[16] Several investigators are now testing this three drug combination and it appears to be as promising as the HEXACAF regimen. Comparative trials of A-C -cis-platinum versus HEXACAF will prove important future clinical investigations.

Ovarian cancer patients who fail to respond to or relapse from primary chemotherapy regimens are known to have an extremely low response rate to secondary treatments. Stanhope et al reported only a 6% overall response rate to second trials of chemotherapy in 360 patients with advanced ovarian carcinoma treated at the M.D. Anderson Hospital and Tumor Institute.[17] More recently, investigators have reported greater success at remission induction in this patient population using different combinations of cis-platinum, hexamethylmelamine, and adriamycin.[18,19,20] Alberts et al have carried out a study of adriamycin-5-fluorouracil-hexamethylmelamine-cis-platinum in patients previously treated with only alkylating agents.[21] Of 18 evaluable patients (at least 1 full treatment course) there have been 6 partial remissions and 1 complete remission for a 39% response rate. One additional patient (6%), showed objective improvement. Median durations of response and survival were 5+ and 10+ months, respectively.

Chemoimmunotherapy. Evidence supporting a possible role for immunotherapy in ovarian cancer includes: 1) ovarian tumor associated antigens;[22] 2) relationship of immunocompetence to survival;[23,24,25] 3) curative immunotherapy in mouse ovarian tumor models;[26] and 4) tumor colony formation by ovarian carcinoma stem cells showing that functioning peritoneal macrophages present within the tumor cell population are required for ovarian colony growth.[2] There are currently a few trials of non-specific immunostimulants in combination with anticancer drugs for the treatment of advanced ovarian cancer. Most of these include C. parvum or Bacillus Calmette Guerin (BCG) as the immunostimulant. One such ongoing study in the Southwest Oncology Group involves the addition of BCG to A-C therapy. As of August 1978, 99 evaluable patients with no prior chemotherapy and measurable stage III, IV or recurrent disease had been randomly assigned to receive A-C or A-C + BCG. Adriamycin, 40 mg/M^2 on day 1 and cyclophosphamide, 200 mg/M^2/day on days 3-6 p.o., were given every 3-4 weeks to a total adriamycin dose of 500 mg/M^2. BCG (Pasteur Institute, 2-3x10^8 viable organisms) was administered by scarification to alternating upper and lower extremity sites on days 8 and 15. There was a similar distribution between the two study arms of patients with Stage IV disease, bulky tumor masses, types of surgical procedures, performance status, prior radiation therapy exposure and histologic types and grades.

The CR + PR rate for A-C + BCG patients of 52% was significantly different ($P < .05$) from the 30% CR + PR rate observed in the A-C group. The median duration of response of 13+ months for the A-C + BCG group was not statistically better than the 7.2 months for the A-C patients. Twenty-eight of 53 or 53% of the A-C patients have died as compared to 15 of 46, or only 33% of the A-C + BCG group. Median survival duration of the A-C + BCG patients (21 months) was statistically better than that of patients receiving only A-C (13.5 months) ($P < .005$). Therapy was well tolerated. There were no drug related deaths and no serious systemic BCG toxicities. Thus, the addition of BCG to the standard A-C treatment for far advanced ovarian carcinoma appeared to have increased response rates, and increased overall survival duration without markedly adding to drug toxicity. Future clinical trails in the Southwest Oncology Group are being planned to continue to test the efficacy of adding BCG to the most active combination chemotherapy regimens.

In Vitro Prediction of Ovarian Cancer Response to Anticancer Drugs. Salmon and his group at the University of Arizona have been using an *in vitro* human tumor stem cell assay to quantitate the sensitivity of an individual patient's cancer to drug therapy.[2,27] Tumor cell suspensions are prepared and 10^6 cells are exposed to varying concentrations of an anticancer drug for 1-24 hours at 37°C. The cells are then washed several times to remove the anticancer drug and a 2 x 10^5 cells are plated on agar in a specialized media. Within 14 days tumor colonies containing 40-80 cells are formed and counted using a dissecting microscope. The number of surviving colonies in the drug treated groups as compared to untreated controls can then be used for assessing sensitivity to the anticancer drug under study. Results proving the assay to be predictive of response in relapse patients were recently published.[27] As of December 1, 1978 we have made 52 *in vitro-in vivo* correlations in 20 ovarian cancer patients. In 45 instances, resistance *in vitro* has successfully predicted clinical resistance, while in 6 instances, the assay has successfully predicted drugs which would induce remission in these relapse patients. In only 1 instance was sensitivity predicted in a patient who proved to be clinically resistant, and there were no instances of *in vitro* resistance and clinical sensitivity. Therefore, the assay appears useful for drug selection, and can most rationally be applied to early high-risk ovarian cancer patients who have not yet received drug treatment.

Therapeutic Conclusions. At the University of Arizona we have developed a flexible but defined therapeutic strategy for the four stages of epithelial-type ovarian cancers. If there are no medical contraindications and except in widely disseminated stage IV disease, all patients undergo bilateral salpingo oophorectomy, total abdominal hysterectomy, omentectomy, radical debulking of pelvic and intraabdominal tumor masses and complete observation of all intraperitoneal surfaces with biopsy and/or cytologic evaluation of suspicious areas. We do not recommend adjuvant radiation therapy or chemotherapy for stage 1A, grade I disease; however, if there has been cyst rupture or evidence of extracystic excrescences, we suggest 6 course of melphalan therapy following following surgery. Patients with stages IB,IC or IIA disease are usually given 12 courses of melphalan therapy, although whole abdominal plus pelvic irradiation is possible alternative. Those with stages IIB or III (with minimal residual tumor) disease have been treated with 12 courses of adriamycin-cyclophosphamide. The teatment of advanced stage III and IV or recurrent disease is less definite. Available therapies with high success rates include the HEXACAF regimen,[6] A-C plus cis-platinum[16,19] and A-C plus BCG.[15]

It must be emphasized that a "second-look" exploratory laparotomy, using the guidelines of the previously discussed initial surgical exploration, is mandatory as an endpoint for therapy in patients who have achieved clinical complete remission. Thus, patients in clinical complete remission with stages IB, IC, IIA, IIB, III and in special instances stage IV disease undergo thorough surgical exploration after the completion of 12-24 months of chemotherapy. Patients with no evidence of disease following thorough "second-look" surgery have greater than an 80% chance of being disease-free at the end of five years.

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Editorials

An Addendum to Excellent Versus Adequate Care: That is the Question

Since the above editorial appeared in the June, 1978 issue of *Arizona Medicine*, the *New England Journal Of Medicine* (Volume 299: pg. 1462) published an interesting editorial entitled, "Medical efficacy versus economic efficiency: A conflict in values" which had a familiary ring. The gist of this editorial written by Drs. William Schwartz and Paul Joscal concerned the "rationing" of medical care which will be the most probable method we have to control the cost of medical care. The key points of the editorial need repetition for they emphasize that *adequate* medical care is apparently what we are going to have to acccept, although it is going to be difficult to establish.

"The public will almost certainly complain angrily about limits imposed on the use of potentially beneficial test and treatments simply because they are not cost justified. Nor will physicians support the attempt. Asking doctors to make decisions by balancing dollars against improved quality or length of life introduces a demand totally alien to our current training and philosophy. Patient protest and physician resistance would probably jeopardize any government policy promoting voluntary commitment to full economic efficiency."

"Understandably no one in public life will be eager to take responsibility for saving dollars by relinquishing potential medical benefits. Those who have proposed to control costs have evaded this issue; they have over-simplified the cost problem by attributing it solely to 'unnecessary' procedures or services provided at high cost. If, as we believe, most expenditures are associated with some benefit, controlling the rise in health care cost through traditional forms of administrative regulation will prove difficult indeed."

In summation the editorial concludes "if excessive utilization proves to be a major component of health expenditures, we cannot control costs without confronting the basic conflict between medical efficacy and economic efficiency."

In other words, someone, somewhere is going to have to make a decision about what we are going to spend our health care dollars on. That person is not going to be popular and thus the decision will be postponed, debated, and ingnored until no further options are available. I would guess that that is going to take approximately ten years to occur, but when it does, the Fourth of July fireworks will in comparison, be just a distant star.

Marshall B. Block, M.D.
Editor

Holistic Health: What is Our Response?

Over the past year, there have been any articles in the lay press about the olistic health movement. Workshops are eing held about every month. In Tucson, e local Holistic Health Association held four day workshop last May which was huge success. About 800 people, mostly nterested laity, heard presentations hich varied from Norman Shealy, M.D., h.D., a neurosurgeon, talking about elf-Help: The Next Great Advance in merican Medicine" to Elizabeth Kübler-oss, M.D., talking about "Life, Death nd Transitions." Popular books on verything from exercise to meditation re dominating the best seller lists. There ppears to be a growing interest in the ublic about their health, coupled with issatisfaction over traditional health are. At the very least, it'is important herefore that physicians become aware f this movement and consciously espond to it.

There is no universally accepted efinition of holistic health. Some of the ost prevalent beliefs about health clude:

(1) Health is a complex, dynamic teraction of the human mind, body, and pirit.

(2) Individuals bear some respons-ility for personal health.

(3) Individuals should be motivated to ork positively for health.

(4) Diverse approaches toward ccomplishing health and treating disease re acceptable if no harm is done and the atient is adequately and honestly ducated.

There is little debate among physicians bout the first three concepts. pplication of these is an idealistic goal oward which all strive. Realistically in a usy medical practice, most physicians all short of adequately dealing with all spects of patient health. We are well-rained to pigeonhole signs and ymptoms efficiently into disease ntities. However, addressing the social nd psychological implications of each ymptom is difficult, time consuming and ersonally draining. We try to achieve full ersonal involvement, but do we do this or all our patients? We make attempts at patient education. How many of us can say that all patients under our care are "actively" striving towards health? Perhaps our failures send people to the confusing and often inaccurate plethora of popular literature to learn about exercise programs, nutrition, stress reduction, relazation exercises, accident consciousness (such as use of seat belts), reduction of cigarette smoking, and ridding our air, food, and water of carcinogens.

The concept of utilizing diverse approaches to health care can be debated. Physicians have a responsibility, however, to educate themselves and take part in the debate. We need to support scientific investigation of alternative health care systems to substantiate or disclaim their hypotheses. Over the last few years, studies have appeared in reputable medical journals on biofeedback, acupuncture and relaxation exercises. As a result, we can now make rational decisions about conditions which might benefit from these treatment modalities. Physicians need to learn what resources are available in their communities and refer for treatment to those disciplines in which we are not skilled. An example is the referral of patients with migraine headaches to a biofeedback center as an adjunct in treatment.

At the University of Arizona College of Medicine, medical students become aware of the holistic health beliefs through the required course in Human Behavior and Development. A seminar elective for senior medical students is available for more independent study. Education and critical analysis is essential to formulating a conscious response to and participation in holistic health ideas. The worst thing we could do is ignore it; ignorance breeds hostility on all sides and only our patients suffer.

Arthur D. Sanders, M.D., Instructor
Department of Amily and
Community Medicine
Louis J. Kettel, M.D., Dean
College of Medicine
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Auxiliary Highlights

The welcoming brochure recently sent by the Arizona Auxiliary to doctors' spouses in the state posed the questions: what is the ArMA Auxiliary, what is the Auxiliary's purpose, what does the Auxiliary do, how are state dues spent, and who can join?

Produced in eye-catching pink by first vice president Mrs. Lynn (Joyce) Newman, it concisely reports the gamut of answers to the above queries. In some part, the following is lifted from the brochure.

Today's more than 1700 members have joined friendly forces since Arizona's 64 organizing wives first met in May of 1930. In the 49 years of its existance, the purpose has remained to assist in the advancment of medicine and public health. The Welfare chairmanship of 1931-33 was soon replaced by Chairmanships in Education and Public Relations; so the purpose translated to: The Improvement of Health Care.

As a state Auxiliary, we coordinate information, programs and education between our parent AMA Auxiliary and the six oranized county Auxiliaries plus members-at-large.

To quote further, the Auxiliary provides leadership training and education material on health related programs and legislative issues. A state newsletter, the Caduceus Crier, communicates among members. Board meetings, open to all members, encourage personal involvement ....

Priority programs such as immunization, hypertension treatment, breast self-exam, V.D., alcohol, drug, and child abuse prevention, concern for the aging, cost containment and health manpower are emphasized, as is working with other community groups. More than 500 sucessful nationwide Auxiliary programs reflect that doctors and their spouses **Care About People**.

State dues are judiciously budgeted to specified categories varying somewhat yearly. General operating takes 22%, the Caduceous Crier 18%, and 39% is distributed among leadership training, national and regional conferences and committee expenses.

All physicians', residents', interns', and medical students' spouses are eligible to join the ArMA Auxiliary. With the remaining 21% of the budget going into state convention and fall conference (community health, family and personal enrichment seminars for all members), why not give thought to the extent of your spouse's participation? Dues themselves are welcomed and serve productive purpose but the Auxiliary would much prefer seeing the person as well.

Since state convention plans are included elsewhere in this issue, this is your opportunity to excercise hero instincts by sharing the printed program and a sense of participation enthusiasm with your spously person.

Mrs. Melvin W. (Jean) Phillips
Auxiliary Editor

THE AMA IS CLOSER TO YOU THAN YOU MIGHT SUPPOSE

An ancient Greek thinker, Diogenes Laertius, wrote "Mountains when far away appear misty . . . but when near at hand they are rugged."

Increased membership in the American Medical Association (up 8,000 in a year's time) refelects the extent to which physicians preceive the ruggedness.

They clearly see the AMA's strength against such dangers as mandatory cost ceilings, over-regulation of health planning, and Frederal Trade Commission actions anent physician advertising and medical-school accreditation. They see the AMA's strength in upholding professional standards, serving the public and profession, and taking voluntary socio-economic initiatives.

But to many non-members, the AMA indeed appears distant and misty. And, that sense of remoteness does not apply only to the national AMA. Doctors in their busy offices and hospitals may feel it toward their state and county societies.

AMA membership at the end of 1978 totaled 210,000 up from 202,000 the previous years. There was a gain from no less than 41 of the states and territories.

Of the 181,000 dues-paying memberships at last year's close, 149,000 were channeled from the state associations and 32,000 were direct.

There are estimates, however, that the total rosters of the state associations exceed that of the AMA by 50,000. Yet the AMA has been greatly expanding and intensifying its help to the states. For example, it has established a Department of Negotiations, malpractice reinsurance company (AMACO), state health legislation unit (which, among other things, drafts model bills), and Department of Federal Communications in recent years.

If more state association members belonged to the national AMA, the latter's $250 regular annual dues could be reduced substantially . . to $200 or less.

The AMA House of Delegates last June slashed dues in half for physicians in their crucial first year of practice. Their membership affords such benefits as computerized placement service, practice-management workshops and guidance, legal counsel, insurance (medical, life, disability, and so forth), as well as a role in staving off federal assaults on their professionalism.

Dr. William H. Welch declared as president of the AMA in 1910:

"Organized effort is a distinguishing mark of modern civilization . . . . We are justified in the confidence that, with the united support and loyalty of the profession, this Association — broadly representative and standing for the best ideals of medical science and art and for professional and civic righteousness — will contribute a benefical share to the working out of our national destiny."

For physicians, this destiny is more at stake now than ever before. And for physicians — new or established, young or old--the need for organized national effort is greater, too.

Let the word be spread that the AMA is A mountain — and not a mist.

Bruce E. Robinson,
Executive Director, ArMA

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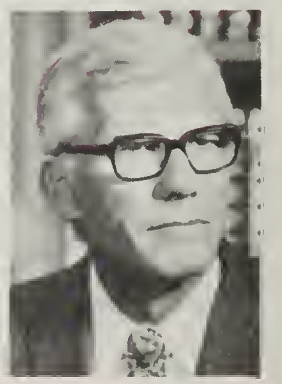
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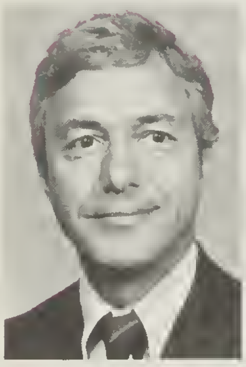
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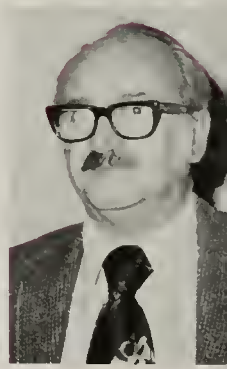
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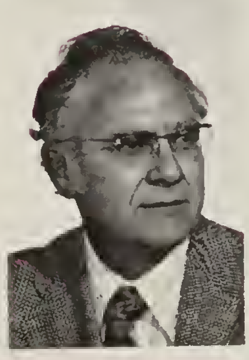

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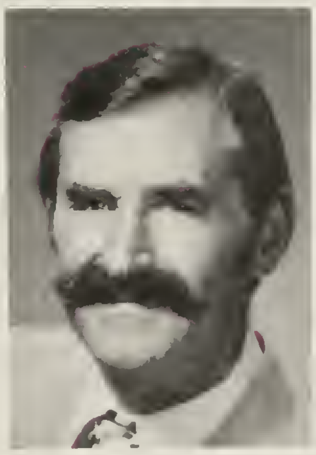

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PROGRAM

Wednesday, April 25, 1979

6:00 A.M. Executive Committee Breakfast .... Lanai Room

8:00 A.M. Board of Directors Meeting .... French Quarter

HOUSE OF DELEGATES

10:00 A.M. First Regular Session .... Convention Center

Call To Order
Robert A. Price, M.D., Speaker

Invocation and Memorial Service

Welcome
Alan A. Gordon, M.D., President
Maricopa County Medical Society

Introduction of Distinguished Guests
Mrs. James L. Parsons, President
Arizona Medical Association Auxiliary

Tom E. Nesbitt, M.D., President
American Medical Association

Introduction of Incoming President
Richard L. Dexter, M.D.

Presidential Address
William E. Crisp, M.D.

Regular Business Session of the House
Refer to the AGENDA section of the
Delegates Manual

2:00 P.M. RESOLUTIONS REFERENCE COMMITTEE .... Sage Room

2:00 P.M. BYLAWS AMENDMENTS REFERENCE COMMITTEE .... Palo Verde Room

Thursday, April 26, 1979

8:00 A.M. "PHYSICIANS FAMILIES" A special program for physicians and their spouses.
See page 5 for details.

12 Noon to 2:00 P.M. SPECIALTY SOCIETY LUNCHEONS
International College of Surgeons .... Lanai Room
Arizona Urological Society .... French Quarter #2

12 Noon PAST PRESIDENT'S LUNCHEON .... French Quarter #1

SPORTS

12 Noon ANNUAL GOLF TOURNAMENT
Orange Tree Golf Club
56th Street & Shea Blvd.
Scottsdale — $23.10 Fee includes Cart & Green Fees.
Registration at the convention is required.

1:00 P.M. ANNUAL TENNIS TOURNAMENT
Paradise Valley Tennis Club
6802 East Northern Avenue, Paradise Valley
$7.00 Fee. Registration at the convention is required.

5:30 P.M. Maricopa County Medical Society Caucus Meeting .... Embassy Room
6:00 P.M. FIFTH ANNUAL NATIONAL CALLIOPE CONCERT .... North Poolside
Courtesy of Boyden L. Crouch, M.D.
7:00 P.M. ANNUAL RECEPTION .... North Poolside
8:00 P.M. PAUL SHANK's FABULOUS STEAK FRY .... North Poolside
Admission by ticket only — Dress: Western & Casual
Featuring: DESERT BLUE GRASS

Friday, April 27, 1979

6:00 A.M. Pima County Medical Society Caucus Breakfast .... Lanai Room

HOUSE OF DELEGATES

8:00 A.M. Second Regular Session .... Convention Center

Refer to the AGENDA section of the Delegates Manual

12 Noon to 2:00 P.M. SPECIALTY SOCIETY LUNCHEONS
Arizona Society of Allergists .... Lanai Room
American College of Surgeons, Arizona Chapter .... French Quarter #1
Arizona Society of Otolaryngology & Maxillo-Facial Surgery .... French Quarter #2
Arizona Psychiatric Society .... French Quarter #3

2:00 P.M. SCIENTIFIC PROGRAM STARTS

FRIDAY AFTERNOON AT A GLANCE

AY	PALO VERDE ROOM Convention Center	SAGE ROOM Convention Center	EMBASSY ROOM Above Hotel Lobby	DIRECTORS ROOM Above Hotel Lobby
	NONSTEROIDAL ANTI—INFLAMMATORY DRUGS Daniel Stechschulte, M.D. *Moderator:* *Thomas F. Hartley, M.D.*	NEW ADVANCES IN ARTHRITIS *A Philip S. Hench Lectureship* Randolph C. Blodgett, M.D. *Moderator:* *Sanford H. Roth, M.D.*	PEDOPHILIA (Child Molesting): DIFFERENTIAL DIAGNOSIS, IDENTIFICATION AND TREATMENTS William S. Gold, M.D. *Moderator:* *John T. Clymer, M.D.*	THE INHERITANCE OF COMMON DISEASE William Horton, M.D. *Moderator:* *Arthur V. Dudley, Jr., M.D.*
		SURGICAL CONSIDERATIONS OF COLD NODULES OF THE THYROIDS Neopito L. Robles, M.D. ***Moderator:*** ***James M. Hurley, M.D.***	*DIET AND COLON CANCER* *Lawrence W. Norton, M.D.* *Moderator:* *Charles E. Henderson, M.D.*	
0 0	RECESS — VISIT EXHIBITS	RECESS - VISIT THE EXHIBITS		RECESS - VISIT THE EXHIBITS

FRIDAY PM	PALO VERDE ROOM Convention Center	SAGE ROOM Convention Center	EMBASSY ROOM Above Hotel Lobby	DIRECTORS ROOM Above Hotel Lobby
3:30 to 4:00	PITUATARY TUMORS: RECENT DIAGNOSTIC AND THERAPEUTIC ADVANCES Marshall B. Block, M.D. William H. White, M.D. Jeffery Black, M.D. *Moderator:* *Wilbur C. Voss, M.D.*	PROLACTIN - AN UPDATE Philip Levy, M.D. *Moderator:* *James M. Hurley, M.D.*	PRIMARY AND SECONDARY HEPATIC TUMORS Charles Putnam, M.D. *Moderator:* *Neopito L. Robles, M.D.*	TUMORS OF THE HEAD NECK and MANAGEMENT OF ORB AND PERIORBITAL PROBLEMS Fernando Kirchner, M.D. *Moderator:* *Floyd K. Berk, M.D.*
4:00 to 4:30	NEW ANTIARRHYTHMIA AGENTS Marvin Dunn, M.D. *Moderator:* *Marvin C. Schneider, M.D.*	UNDERSTANDING AND TREATING CHRONIC PAIN — A PROFESSIONAL CHALLENGE Presentor: Robert H. Barnes, M.D. Co-author Robert B. Poser, M.D. *Moderator:* *James M. Hurley, M.D.*	VASCULAR MONITORING TECHNIQUES Casey D. Blitt, M.D. *Moderator:* *Neopito L. Robles, M.D.*	
4:30 to 5:00		SLEEP APNEA SYNDROME: OBSERVATIONS ON A RECENTLY DESCRIBED COMMON CLINICAL PROBLEM Presentor: Richard M. Riedy, M.D Co-Author: Bernard E. Levine, M.D. *Moderator:* *James M. Hurley, M.D.*	ADULT RESPIRATORY DISTRESS SYNDROME Charles W. Otto, M.D. *Moderator:* *Arthur V. Dudley, Jr., M.D.*	

7:00 P.M.	ArMPAC RECEPTION	....	Convention Center
8:00 P.M.	ArMPAC ANNUAL BANQUET	....	Convention Center

Saturday, April 28, 1979

7:00 A.M. BREAKFAST .... French Quarter

7:30 A.M. to 8:45 A.M. BREAKFAST PROGRAM FOR PHYSICIANS AND SPOUSES .... French Quarter
Title: THE INHERITANCE OF ALCOHOLISM
Donald Goodwin, M.D.
Professor & Chairman, Department of Psychiatry
The University of Kansas Medical Center
Moderator: Marvin C. Schneider, M.D.

9:00 A.M. SCIENTIFIC PROGRAM STARTS

ATURDAY MORNING AT A GLANCE

TUR.	PALO VERDE ROOM Convention Center	SAGE ROOM Convention Center	EMBASSY ROOM Above Hotel Lobby	DIRECTORS ROOM Above Hotel Lobby
0 0))0	WHAT'S NEW IN ENDOCRINOLOGY AND METABOLISM *a day long course starting at 9 AM and concluding at 5 PM* R. NEIL SCHIMKE, M.D. + DIABETES MELLITUS A GENETICALLY HETEROGENEOUS DISEASE + POLYGLANDULAR SYNDROMES + PRIMARY AMENORRHEA *Moderator: Philip Levy, M.D.*	THE ESTROGEN CONTROVERSY - TO GIVE OR NOT TO GIVE Kermit Krantz, M.D. *Moderator: Peter Mao, M.D.*	DRUGS USED IN THE TREATMENT OF PSYCHIATRIC ILLNESS - Panel James E. Campbell, M.D. Stuart M. Gould, M.D. Harris D. Murley, M.D.	THE DAMAGED JOINT - HOW AND WHEN TO REPAIR Fred Reckling, M.D. *Moderator:* *Stephen R. Stein, M.D.*
)0 30		*THE ADOLESCENT IN PREGNANCY* *Kermit Krantz, M.D.* Moderator: Peter Mao, M.D.	WHAT IS AN APPROPRIATE HYPERTENSION WORK-UP? Ray W. Gifford, Jr., M.D. *Moderator:* *W. Scott Chisholm, Jr., M.D.*	URTICARIA - Etiology, Pathogenesis & Treatment Bryan R. Updegraff, M.D. *Moderator:* *Arthur V. Dudley, Jr., M.D.*
30)0	RECESS - VISIT EXHIBITS		RECESS - VISIT EXHIBITS	
)0 30 30 Noon	WHAT'S NEW IN ENDROCRINOLOGY AND METABOLISM - continued JOSEPH KYNER, M.D. + *MANAGEMENT OF THE COMPLEX DIABETIC* + *HASHIMOTO'S OR GRAVES' DISEASE - DIAGNOSTIC DILEMMA* + *CUSHING'S DISEASE - NEW CONCEPTS IN MANAGEMENT* *Moderator:* *Philip Levy, M.D.*	MEDICAL MANAGEMENT OF ANGINA Marvin Dunn, M.D. *Moderator:* *Richard L. Dexter, M.d.*	BIRTH CONTROL PILLS - USE AND ABUSE Charles King, M.D. *Moderator:* *W. Scott Chisholm, Jr., M.D.*	A SIMPLIFIED APPROACH TO ENT SURGERY Fernando Kirchner, M.D. *Moderator:* *Floyd K. Berk, M.D.*

12 Noon to 2:00 P.M.	SPECIALTY SOCIETY LUNCHEONS Arizona Society of Internal Medicine American College of Obstetricians and Gynecologists	 Lanai Room French Quarter #1

SATURDAY AFTERNOON AT A GLANCE

SATUR PM	PALO VERDE ROOM Convention Center	SAGE ROOM Convention Center	EMBASSY ROOM Above Hotel Lobby	DIRECTORS ROOM Above Hotel Lobby
2:00 to 2:30	WHAT'S NEW IN ENDOCRINOLOGY AND METABOLISM *9 AM and concluding at 5 PM* JOSPEH KYNER, M.D. - cont. + *MANAGEMENT OF THE COMPLEX DIABETIC* + *HASHIMOTO'S OR GRAVES' DISEASE - DIAGNOSTIC DILEMMA* + *CUSHING'S DISEASE - NEW CONCEPTS IN MANAGEMENT* *Moderator:* *Philip Levy, M.D.*	COMMON ATHLETIC INJURIES Fred Reckling, M.D. *Moderator:* *Stephen R. Stein, M.D.*	MANAGEMENT OF GYNECOLOGIC CANCER Charles King, M.D. *Moderator:* *Peter Mao, M.D.*	DIABETES MELLITUS GENETICALLY HETE GENEOUS DISEASE R. Neil Schimke, M.D. *Moderator:* *Arthur V. Dudley, Jr.,*
2:30 to 3:00				
3:00 to 3:30	RECESS - VISIT EXHIBITS	RECESS - VISIT EXHIBITS		RECESS - VISIT EXHIBITS
3:30 to 4:00	WHAT'S NEW IN ENDOCRINOLOGY AND METABOLISM - continued BARBARA LUKERT, M.C. + *THE HYPERLIPIDEMIAS* + *METABOLIC BONE DISEASE* + *THE OBESE PATIENT*	POLYGLANDULAR SUNDROMES R. Neil Schimke, M.D. *Moderator:* *W. Scott Chisholm, Jr., M.D.*	NEW CONCEPTS IN THE TREATMENT OF SHOCK Marvin Dunn, M.D. *Moderator:* *Richard L. Dexter, M.D.*	SECONDARY AMENOR Charles King, M.D. *Moderator:* *Peter Mao, M.D.*
4:00 to 4:30		MANAGEMENT OF THE COMPLEX DIABETIC Joseph Kyner, M.D. *Moderator:* *W. Scott Chisholm, Jr., M.D.*		
4:30 to 5:00	Moderator: Philip Levy, M.D.	HASHIMOTO'S DISEASE OR GRAVES' DISEASE - DIAGNOSTIC DILEMMA Joseph Kyner, M.D. *Moderator:* *W. Scott Chisholm, Jr., M.D.*	MEDICAL MANAGEMENT OF THE HYPERSENSITIVE PATIENT Ray W. Gifford, Jr., M.D. *Moderator:* *Suresh C. Anand, M.D.*	CURRENT MANAGEME HIP FRACTURES Fred Reckling, M.D. *Moderator:* *Arthur V. Dudley, Jr.,*

7:00 P.M. PRESIDENT'S RECEPTION .... North Poolside
8:00 P.M. PRESIDENT'S BANQUET .... Convention Center
Guest Speaker: Astronaut Edgar D. Mitchell, Sc.D.
Title: THE EMERGINE HUMAN

Sunday, April 29, 1979

7:00 A.M. BREAKFAST . . . . French Quarter

7:30 A.M.
to
8:45 A.M. BREAKFAST PROGRAM FOR PHYSICIANS AND SPOUSES . . . . French Quarter
Title: SEX, SCIENCE AND RELIGION
Kermit Krantz, M.D.
Professor & Chairman
Department of Obstetrics & Gynecology
The University of Kansas Medical Center
Moderator: William C. Scott, M.D.

9:00 A.M. SCIENTIFIC PROGRAM STARTS

SUNDAY MORNING AT A GLANCE

UNDAY M	PALO VERDE ROOM Convention Center	SAGE ROOM Convention Center	EMBASSY ROOM Above Hotel Lobby	DIRECTORS ROOM Above Hotel Lobby
:00 o :30	NEW CONCEPTS IN AUTOIMMUNE DISEASE Daniel Stechschulte, M.D. *Moderator: Marvin C. Schneider, M.D.*	A NEW APPLICATION OF EKG TREADMILL TESTING OF THE ELDERLY FOR EXERCISE PRESCRIPTION WITH FOLLOW-UP TEST RESULTS Julius Schwimmer, M.D. *Moderator: Charles E. Henderson, M.D.*	SYMPTOMS, SIGNS AND TREATMENT OF SLOW GASTRIC EMPTYING James Rhodes, M.D. *Moderator: Suresh C. Anand, M.D.*	THE ROLE OF GENETICS IN CLINICAL MEDICINE William Horton, M.D. *Moderator: William C. Scott, M.D.*
:30 o 0:00		LEGIONNAIRE'S DISEASE - UPDATE Karen M. Starko, M.D. *Moderator: Luis S. Tan, M.D.*		
0:00 o 0:30	ARTHRIOSCOPIC KNEE SURGERY Eugene J. Chandler, M.D. *Moderator: Charles E. Henderson, M.D.*	PRESURGICAL EVALUATION OF PATIENTS WITH RECURRENT PANCREATITIS: EMPHASIS ON THE VALUE OF ERCP George E. Burdick, M.D. *Moderator: Neopito L. Robles, M.D.*	THE SPECTRUM OF ESOPHAGEAL REFLUX - DIAGNOSIS AND MANAGEMENT James Rhodes, M.D. *Moderator: Marvin C. Scheider, M.D.*	LONG-TERM INTERMITTANT OXYGEN THERAPY - A NEW METHOD W. Sam Williams, M.D. *Moderator: William C. Scott, M.D.*
0:30 o 1:00	RECESS - VISIT EXHIBITS	RECESS - VISIT EXHIBITS		RECESS - VISIT EXHIBITS

SUNDAY AM	PALO VERDE ROOM Convention Center	SAGE ROOM Convention Center	EMBASSY ROOM Above Hotel Lobby	DIRECTORS ROOM Above Hotel Lobby
11:00 to 11:30	MALABSORPTION - FIVE USEFUL TESTS, WHAT THEY MEAN AND WHAT THEY MEASURE James Rhodes, M.D. *Moderator: Luis S. Tan, M.D.*	THE HYPERLIPIDEMIAS Barbara Lukert, M.D. *Moderator: Thomas F. Hartley, M.D.*	IS YOUR PATIENT REALLY ALLERGIC? Daniel Stechschulte, M.D. *Moderator: Marvin C. Schneider, M.D.*	ANXIETY NEUROSIS Donald Goodwin, M.D. *Moderator: John T. Clymer, M.D.*
11:30 to 12 Noon		THE OBESE PATIENT Barbara Lukert, M.D. *Moderator: Thomas F. Hartley, M.D.*		

SPECIALTY SOCIETY MEETINGS

THURSDAY

International College of Surgeons
12 Noon .... Lanai Room

Arizona Urological Society
12 Noon .... French Quarter #2

FRIDAY

Arizona Society of Allergists
12 Noon .... Lanai Room

American College of Surgeons, Arizona Chapter
12 Noon .... French Quarter #1

Arizona Society of Otolaryngology & Maxillo-Facial Surgery
12 Noon .... French Quarter #2

Arizona Psychiatric Society
12 Noon .... French Quarter #3

Arizona Thoracic Society
12 Noon .... Kudu Room

SATURDAY

Arizona Society of Internal Medicine
12 Noon .... Lanai Room

American College of Obstetricians and Gynecologists
12 Noon .... French Quarter #1

Guest Speakers

ELLEN M. BERMAN, M.D.
Associate Professor
of Psychiatry
Department of Psychiatry
University of Pennsylvania
School of Medicine

PERRY A BERMAN, M.D.
Private Practice of Psychiatry
and Part-Time Consultant
in Forensic Psychiatry,
Defenders Association,
Philadelphia

CASEY D. BLITT, M.D.
Tucson

MARSHALL B. BLOCK, M.D.
Phoenix

GEORGE E. BURDICK, M.D.
Phoenix

JAMES E. CAMPBELL, M.D.
Phoenix

MARVIN DUNN, M.D.
Professor of Medicine
(Immunology-Rheumatology)
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

ALFRED S. GERVIN, M.D.
Tucson

RAY W. GIFFORD, JR., M.D.
Department of Hypertension
and Nephrology
Cleveland Clinic Foundation

WILLARD S. GOLD, M.D.
Tucson

DONALD GOODWIN, M.D.
Professor & Chairman,
Department of Psychiatry
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

STUART M. GOULD, M.D.
Phoenix

WILLIAM HORTON, M.D.
Assistant Professor of Medicine
and Pediatrics
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

CHARLES KING, M.D.
Assistant Professor of
Obstetrics and Gynecology
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

FERNANDO KIRCHNER, M.D.
Professor of Otolaryngology
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

KERMIT KRANTZ, M.D.
Professor & Chairman,
Department of Obstetrics
and Gynecology
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

JOSEPH KYNER, M.D.
Associate Professor of Medicine
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

BARBARA LUKERT, M.D.
Associate Professor of Medicine
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

HARRIS D. MURLEY, M.D.
Phoenix

LAWRENCE W. NORTON, M.D.
Tucson

CHARLES W. OTTO, M.D.
Tucson

CHARLES PUTNAM, M.D.
Tucson

FRED RECKLING, M.D.
Professor of Surgery
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

JAMES RHODES, M.D.
Associate Professor of Medicine
and Physiology
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

R. NEIL SCHIMKE, M.D.
Professor of Medicine
and Pediatrics
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

JULIUS SCHWIMMER, M.D.
Sun City

KAREN M. STARKO, M.D.
Phoenix

DANIEL STECHSCHULTE, M.D.
Professor of Medicine
(Immunology-Rheumatology)
College of Health Sciences
and Hospital
The University of Kansas
Medical Center

BRYAN R. UPDEGRAFF, M.D.
Sun City

W. SAM WILLIAMS, M.D., F.A.C.P.
Scottsdale

Tom E. Nesbitt, M.D.
President
American Medical Association
Dr. Nesbitt will address the
House of Delegates on
Wednesday, April 25, 1979
at 10:00 AM

Arizona Medical Association Auxiliary

Presidents

Mrs. John T. Clymer
1979-80

Mrs. James L. Parsons
1978-79

Convention Chairman

Mrs. Dino Di Censo

Co-Chairman — Mrs. Stephen Kaster

PROGRAM

WEDNESDAY — April 25, 1979

9:00 a.m. - 12 Noon	Deliver arts and crafts to Safari Convention Center	
10:00 a.m.	ArMA House of Delegates First Meeting ArMA Auxiliary President's Address Mrs. James L. Parsons	Safari Convention Center
1:00 p.m. - 4:00 p.m.	Registration	Safari Convention Center
1:00 p.m. - 4:00 p.m.	Hospitality Center	Safari Convention Center
1:00 p.m. - 4:00 p.m.	"Creative Moments" (Arts & Crafts)	Safari Convention Center

Noon	Gavel Club Luncheon Past Presidents Mrs. George L. Hoffman	Chez Louis — Scottsdale Mall
3:00 p.m.	Executive Committee Meeting	Safari Resort — President's Room

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FRIDAY — April 27, 1979

9:00 a.m. - 11:00 a.m.	Registration	Safari Convention Center
9:00 a.m. - 11:00 a.m.	Hospitality Center	Safari Convention Center
9:00 a.m. - 3:30 p.m.	"Creative Moments" (Arts & Crafts) Pick items up between 2:30 p.m. & 3:30 p.m. at Convention Center.	Safari Convention Center
8:00 a.m.	Continental Breakfast	Scottsdale Sheraton Hotel
8:30 a.m. - 11:30 a.m.	Annual Meeting and Election of Officers Conducted by Mrs. James L. Parsons — Open to all members — plan to attend!	Scottsdale Sheraton Hotel
12:00 p.m. - 2:00 p.m.	Installation Luncheon & Fashion Show Mrs. James L. Parsons presiding ArMA President's Address by William Crisp, M.D. Installation of Officers by AMA Auxiliary Director, Mrs. Howard Kimball	Casa Blanca Inn

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THURSDAY — April 26, 1979

8:00 a.m. - 4:00 p.m.	Registration	Safari Convention Center
9:00 a.m. - 4:00 p.m.	Hospitality Center	Safari Convention Center
9:00 a.m. - 4:00 p.m.	"Creative Moments" (Arts & Crafts)	Safari Convention Center
8:00 a.m. - 11:30 a.m.	"Physicians' Families" A special program for physicians and their spouses. Guest Speakers: Ellen Berman, M.D. Perry Berman, M.D. Overview — Followed by group discussions.	Safari Convention Center
12:00 p.m. - 2:00 p.m.	Luncheon Guest Speaker: Ellen Berman, M.D. Topic: "Adult Development and Marital Stress"	Scottsdale Sheraton Hotel
2:15 p.m.	General Board Meeting Mrs. James L. Parsons presiding	Scottsdale Sheraton Hotel
6:00 p.m.	Fifth Annual National Calliope Concert	Safari — North Poolside
7:00 p.m.	Reception and Steak Fry with lots of fun!	Safari — North Poolside

7:00 p.m.	ArMPAC Reception & Banquet	Safari Convention Center

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SATURDAY — April 28, 1979

7:00 a.m.	ArMA Breakfast Panel — Spouses welcome. Guest Speaker: Donald Goodwin, M.D. Topic: "Inheritance of Alcoholism"	Safari French Quarter
9:00 a.m. - Noon	Positive Fun for Everyone! Pre-registration recommended	Scottsdale Sheraton Hotel
9:00 a.m.	Continental Breakfast	
9:30 a.m. - 10:30 a.m.	Room A — Chinese Cooking Demonstration Mrs. Peter Mao Registration limited to 25. $5.00 donation to AMA-ERF at time of registration. Room B — "Recycling R.N.'s" Panel Discussion Mrs. John Sebald Mesa Community College Department of Nursing Edithe Stellhorn Arizona State University Department of Nursing	
10:45 a.m. - 11:45 a.m.	Room A — Chinese Cooking Demonstration Mrs. Peter Mao Registration limited to 25. $5.00 donation to AMA-ERF at time of registration. Room B — "Where is Woman's Place?" Panel Discussion Mrs. George Drach Mrs. Glen Hait Room C — "Battle of the Bulge" Exercise Instruction Mrs. Ralph Linden	
7:00 p.m.	President's Reception	Safari — North Poolside
8:00 p.m.	President's Banquet Guest Speaker: Astronaut Edgar Mitchell, M.D. Topic: "The Emergine Human"	Safari Convention Center

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SUNDAY — April 29, 1979

7:00 a.m. - 9:00 a.m.	ArMA Breakfast Panel Spouses welcome. Guest Speaker: Kermit Krantz, M.D. Topic: "Sex, Science and Religion"	Safari French Quarter
Noon	Convention closes.	

NEW DIRECTIONS

Physicians' Families

A Special Program for Arizona's Doctors & Spouses
at the 1979 Annual Meeting

Arizona Medical Association and Auxiliary
April 25 - 29 — Safari Convention Center, Scottsdale

Thursday Morning, April 26, 1979

8:00 a.m. Opening Presentation — A survey of common problems confronting professional families today, leading into a presentation of some problems unique to physicians and their families

Ellen Berman, M.D. and Perry Berman, M.D.

Ellen Berman is director of Clinical Training, Marriage Council of Philadelphia and Associate Professor Psychiatry, University of Pennsylvania. Perry Berman is in the private practice of psychiatry. They bring to this meeting their personal experience in handling the stresses of being in a professional family.

8:45 a.m. Coffee break

9:00 a.m. Group discussions — To further define some of the problems concerning Arizona families and provide an opportunity for open discussion of these problems.

Discussion leaders:

Hal J. Breen, M.D.
David S. Burgoyne, M.D.
Murray M. DeArmond, M.D.
James G. Hill, M.D.
Derald G. May, M.D.
Dennis C. Westin, M.D.

10:45 a.m. Summing up — A chance for each group to report on issues discussed. Comments by Drs. Berman.

11:30 a.m. Adjournment

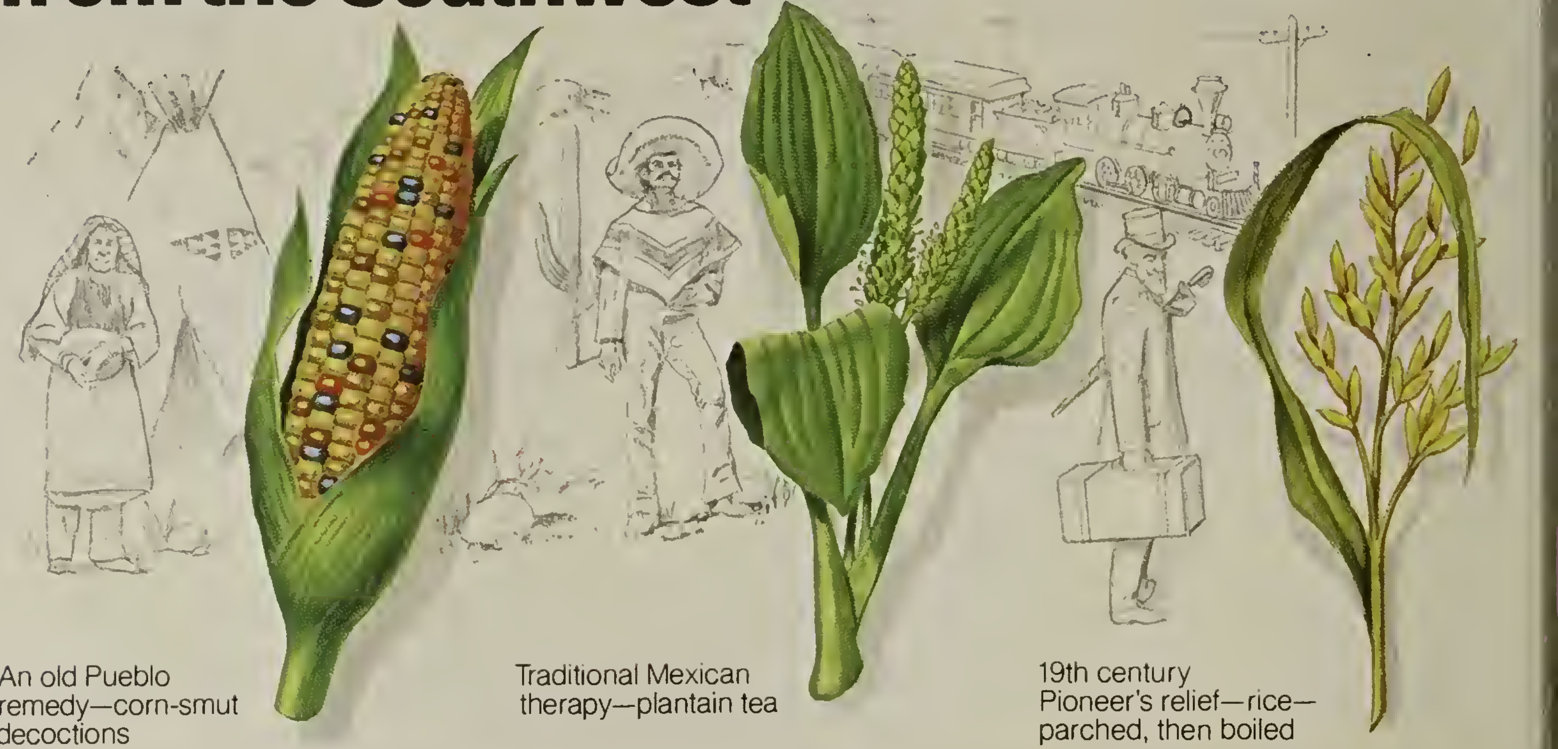
Please pre-register us for this program — no fee required.
Please print both husband's and wife's names.

Mail To: Physicians' Families Program
Arizona Medical Association, Inc.
810 W. Bethany Home Road
Phoenix, AZ 84013

This program accredited for 3 hours of Category 1 CME credit by ArMA.

For nonnarcoti

Yesterday's folk remedies from the Southwest



An old Pueblo remedy—corn-smut decoctions

Traditional Mexican therapy—plantain tea

19th century Pioneer's relief—rice—parched, then boiled

ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

Board of Directors

The meeting of the Board of Directors of the Arizona Medical Association, Inc. held dat 810 W. Bethany Home Rd., Phoenix, Arizona on Saturday, December 16, 1978, a quorum being present, convened at 10:09 a.m., Richard L. Dexter, M.D., President and Chairman, presiding.

ArMPAC

Report

Dr. Austin reported that ArMPAC has been very active in the recent election, having done an in-depth study regarding all candidates, determining who would best support the needs of the medical profession, and supporting 40 of the 60 races, being uniformly sucessful in the final results.

Dr. Austin also informed the Board that all documents requested under the FEC subpoena had been supplied but that no final determination had been received regarding ArMPAC/AMPAC contributions.

In response to a request of the membership for a definition of the relationship between ArMA and ArMPAC, Dr Austin advised the board that pursuant to legal opinion, ArMA may appoint management of ArMPAC; that ArMA may exercise control over ArMPAC; and that the President of ArMA, with concurrence of the Board of Directors, will appoint the chairman and member of ArMPAC.

Chairman's Resignation

Dr. Austin advised that on January 6, 1979, he would be leaving to resume active duty with the United States Navy in Guam for a two-year period and submitted to the Board his resignation as Chairman of ArMPAC.

IT WAS MOVED AND CARRIED TO ACCEPT THE REPORT AS GIVEN AND THE RESIGNATION OF JAMES A. AUSTIN, M.D., AS CHAIRMAN OF ArMPAC AND TO APPOINT, CONTINGENT UPON HER ACCEPTANCE, MARY ANN JOHNSON AS CHAIRMAN FOR COMPLETION OF THE EXISTING TERM.

Board of Directors

Resignation - Southeastern District Director

IT WAS MOVED AND CARRIE ACCEPTING THE RESIGNATION O EDWARD R. CURTIS, M.D., A SOUTHEASTERN DISTRIC DIRECTOR AND TO SOLICIT NOMINATIONS FROM THE COUNTIES O COCHISE, GRAHAM, GREENLE AND SANTA CRUZ, WITH SAI NOMINATION TO BE CONSIDERE AND ACTED UPON BY THE BOAR OF DIRECTORS AT ITS MEETING ON FEBRUARY 10, 1979.

Frederick W. Kelly Lawsuit

Edward Jacobson, counsel for th Association, addressed the Boar regarding the lawsuit filed by Frederick W. Kelly, field October 22, 1978, and th Motion to Dismiss filed on behalf o ArMA, advising the Board that the Hon William P. French had, in fact, dismisss the lawsuit on December 15, 1978

"Focus on Positive Health Strategies' Conference

Report of William E. Crisp, M.D RECIVED.

Resolution 7-78

Coconino County Medical Society' activities RECEIVED.

Legal Expenses - Attorney General Demands

Letter of December 1, 1978, from Coconino County Medical Society

control of diarrhea

Clinical therapy for today

Cantil® 25 mg. tablets 25 mg./5 ml. liquid (mepenzolate bromide NF)

As nonnarcotic as these folk remedies of yesterday, Cantil is a logical clinical choice in the adjunctive management of diarrhea* today.

- **Nonnarcotic**—no physical dependence and no potential embarrassment to the patient traveling abroad. And you can prescribe it over the phone.
- **Anticholinergic†**—helps relieve spasm and resulting cramping and other abdominal discomfort that often accompanies diarrhea.
- **Available in 25 mg. tablets**—a convenience for patients who are traveling or working. And Cantil is economical.

Cantil...control that's convenient and nonnarcotic

Merrell

*This drug has been classified as "possibly" effective as an adjunct in the treatment of diarrhea.

†See Contraindications, Precautions, Warnings, and Adverse Reactions

See prescribing information on the following page.

regarding contribution by it to the legal expenses incurred in connection with the Attorney General's recent demands RECEIVED.

Joseph B. Goldberger Award in Clinical Nutrition

Acknowledgment of our nomination of Mervyn D. Willard, M.D. RECEIVED.

Benjamin Rush Bicentennial Award for Citzenship & Community Service.

Acknowledgment of our nomination of Glenn M. Friedman, M.D. and notice that award went to Representative Tim Lee Carter, M.D. of Kentucky and Washington, D.C. RECEIVED.

Fifty Year Club

IT WAS MOVED AND CARRIED THAT FIFTY YEAR CLUB AWARDS BE PRESENTED DURING THE 1979 ANNUAL MEETING OF THE ASSOCIATION TO ROY EARLE BURGESS, M.D. AND DONALD F. HILL, M.D.

Federal Trade Commission

AMA Mailgram of 11/30/78 relating to FTC action regarding the AMA, advertising and patient solicitation RECEIVED

IRS Audit

IRS letter dated 11/24/78 regarding status of 1975 audit RECEIVED.

Resignation - Central District Director

IT WAS MOVED AND CARRIED ACCEPTING THE RESIGNATION OF JAMES A. AUSTIN, M.D., AS CENTRAL DISTRICT DIRECTOR AND TO SOLICIT NOMINATIONS FROM MARICOPA COUNTY, WITH SAID NOMINATION TO BE CONSIDERED AND ACTED UPON BY THE BOARD OF DIRECTORS AT ITS MEETING ON FEBRUARY 10 1979.

EXECUTIVE COMMITTEE

Membership Classification Changes Approved

Maricopa County Medical Society:

1. Charles E. Borah, M.D. - Active to Associate -Account retirement - Effective 12/16/78 - Dues Exempt.
2. Edward L. Compere, M.D. - Active Over 70 to Associate - Account Retirment - Effective 12/16/78 - Dues Exempt.
3. Arthur F. Dorner, M.D. - Active Over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
4. Robert B. Ellis, M.D. - Active Over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
5. R. Lee Foster, M.D. - Active Over 70 to Associate -Account Retirement - Effective 12/16/78 - Dues Exempt.
6. Perry H. Jacobs, M.D. - Active Over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
7. Artell E. Johnson, M.D. - Active over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
8. Leonard Jourdonais, M.D. - Active Over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
9. Carl T. Kirchmaier, M.D. - Active Over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
10. Maurice R. Richter, M.D. - Active Over 70 to Associate - Account Retirement - Effective 12/16/78 - Dues Exempt.
11. Reed D. Shupe, M.D. - Active Over 70 to Associate -Account Retirement - Effective 12/16/78 - Dues Exempt.
12. Durand Smith, M.D. - Active over 70 to Associate -Account Retirement - Effective 12/16/78 - Dues Exempt.
13. Robert D. Smith, M.D. - Active Over 70 to Associate -Account Retirement - Effetive 12/16/78 - Dues Exempt.
14. Lloyd K. Swasey, M.D. - Active Over 70 to Associate -Account Retirement - Effective 12/16/78 - Dues Exempt.
15. Albert Eckstein, M.D. - Active to Active Over 70 -Account Age - Effective 1/1/79 - Dues Exempt.
16. James O. Fuzzell, M.D. - Active to Affiliate -Account Missionary Work - Effective 1/1/79 - Dues Exempt.

Cantil®
(mepenzolate bromide NF)

Tablets and Liquid
AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

INDICATIONS: Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Effective": Cantil is indicated for use as adjunctive therapy in the treatment of peptic ulcer

"Probably" effective. Cantil is indicated for use as adjunctive therapy in the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis, acute enterocolitis and functional gastrointestinal disorders) and in neurogenic bowel disturbances (including the splenic flexure syndrome and neurogenic colon).

"Possibly" effective: Cantil is indicated as an adjunct in the treatment of diverticulitis and mild ulcerative colitis. Cantil is also indicated as an adjunct in the treatment of diarrheas, i.e., loose stools, functional diarrheas, post-gastrectomy diarrheas (post-gastrectomy syndrome, dumping syndrome), drug induced diarrheas, acute enteritis, intestinal viral infection, colitis, ileocolitis and diarrheas with ileostomies and ileoanal anastomoses.

To be effective the dosage of Cantil must be titrated to the individual patient's needs.

Final classification of the less-than-effective indications requires further investigation

IT SHOULD BE NOTED AT THIS POINT IN TIME THAT THERE IS A LACK OF CONCURRENCE AS TO THE VALUE OF ANTICHOLINERGICS IN THE TREATMENT OF GASTRIC ULCER.

IT HAS NOT BEEN SHOWN CONCLUSIVELY WHETHER ANTICHOLINERGIC DRUGS AID IN THE HEALING OF A PEPTIC ULCER, DECREASE THE RATE OF RECURRENCES OR PREVENT COMPLICATION

THESE FUNCTIONAL GASTROINTESTINAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS, ETC.

CONTRAINDICATIONS: 1. In glaucoma (particularly narrow-angle) 2. In obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy). 3. In obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis, etc) 4 In paralytic ileus. 5 In intestinal atony of the elderly or debilitated patient. 6 In severe ulcerative colitis and toxic megacolon complicating ulcerative colitis. 7. In acute hemorrhage where the cardiovascular status is unstable 8 In myasthenia gravis
WARNINGS: 1. An early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy, may be diarrhea. Treatment with mepenzolate bromide in this instance would be inappropriate and possibly harmful 2. Heat prostration (fever and heat stroke due to decreased sweating) may occur with use of this drug in the presence of high environmental temperature. 3. The patient should be warned not to engage in activities requiring mental alertness such as operating machinery or driving a motor vehicle if drowsiness or blurred vision occurs 4 Since the safety of this drug in pregnancy has not been established, use of this drug in such patients requires that the potential benefits of the drug be weighed against possible hazards to the mother and child
PRECAUTIONS: Cantil should be used with caution in patients in which the anticholinergic effects might produce adverse effects, such as in open-angle glaucoma (contraindicated in narrow-angle), autonomic neuropathy, non-obstructing prostatic hypertrophy and hiatal hernia associated with reflux esophagitis In the treatment of gastric ulcer the use of anticholinergic drugs may produce a delay in gastric emptying time and may complicate such therapy (antral stasis). In ulcerative colitis large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon Use with caution in patients with hepatic or renal disease. Do not rely on the use of this drug in the presence of complications of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate Use with caution in patients with hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias and hypertension. With overdosage, a curare-like action may occur.
ADVERSE REACTIONS: Anticholinergic drugs produce certain effects which may be physiologic or toxic depending upon the individual patient's response The physician must delineate these. Adverse reactions may include dryness of the mouth; urinary hesitancy and retention; blurred vision and tachycardia, palpitations; mydriasis; dilation of the pupil; cycloplegia, increased ocular tension; loss of taste, headaches, nervousness, drowsiness, weakness; dizziness; insomnia, nausea, vomiting, impotency, suppression of lactation; constipation; bloated feeling, severe allergic reaction or drug idiosyncrasies, including anaphylaxis, urticaria and other dermal manifestations; some degree of mental confusion and/or excitement especially in elderly persons Decreased sweating is another adverse reaction that may occur. It should be noted that adrenergic innervation of the eccrine sweat glands on the palms and soles make complete control of sweating impossible. An end point of complete anhidrosis cannot occur because large doses of drug would be required and this would produce severe side effects of parasympathetic paralysis.
DOSAGE AND ADMINISTRATION: Cantil Tablets: Usual Adult Dose One or 2 tablets three times a day preferably with meals and 1 or 2 tablets at bedtime.. Begin with the lower dosage when possible and adjust subsequently according to the patient's response
Cantil Liquid: Usual Adult Dose: One or 2 teaspoonfuls three times a day preferably with meals and 1 or 2 teaspoonfuls at bedtime. As with the tablets, begin with the lower dosage when possible and adjust subsequently according to the patient's response.
DRUG INTERACTIONS: Concomitant administration of anticholinergic drugs and any other drugs which would increase the anticholinergic effects of Cantil is to be avoided
MANAGEMENT OF OVERDOSAGE: With overdosage a curare-like action may occur. Symptomatic treatment of overdosage is directed to the anticholinergic effects of the drug Severe intoxication with oral overdosage of Cantil is unlikely, since, being a quaternary anticholinergic, passage across the blood brain barrier is not known to occur If severe symptoms do occur, gastric lavage should be instituted promptly Physostigmine or other reversible anticholinesterases may be necessary Symptomatic treatment should also be instituted.

(Revised January, 1975)

Merrell

MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215, U.S.A.

8-4172 (Y659A)

17. Jerome Gerendasy, M.D. - Active
Associate -Account Illness - Effecti
1/1/79 - Dues Exempt.
18. Leslie Kober, M.D. - Active Over
to Associate -Account Retirement
Effective 12/16/78 - Dues Exempt.
19. Norman Ross, M.D. - Active Ov
70 to Associate -Account Residency-
Effective 11/1/78 - Dues Exempt.
20. Stephen M. Lantz, M.D. - Active
Associate - Account Residency - Effecti
11/1/78 - Dues exempt. ·
21. Thomas Ross, M.D. - Active
Associate - Account Residency - Effecti
11/17/78 - Dues Exempt.
22. A.G. Wagner, M.D. - Active
Active Over 70 - Account Age - Effecti
11/17/78 - Dues Exempt.

Pima County Medical Society:
1. Emery E. Royce, M.D. - Active
Associate - Account Retirement
Effective 12/16/78 - Dues Exempt.
2. Solomon Cutcher, M.D. - Active
Affiliate -Account Moved out of Stat
Effective 12/16/78 - Dues Exempt.
3. Emery Bolgar, M.D. - Associate
Account Retired -Effective 12/16/78
Dues Exempt.
4. Norman W. Flaherty, M.D.
Associate - Account Retired - Effecti
12/16/78 - Dues Exempt.

Yavapai County Medical Society:
1. Ernest A. Born, M.D. - Active
Associate -Account Retirement
Effective 12/16/78 - Dues Exempt.

Yuma County Medical Society:
1. Russell Bloomdahl, P.A. - Affiliat
Effective 12/16/78

Memberships Approved

Student Members:
1. Mary Decker
2. Mary Saufferer
3. Charlotte Richards

BENEVOLENT AND LOAN FUN COMMITTEE

Thank you letter from Mark S. Wurz dated 10/13/78 — Received.

FINANCE COMMITTEE

Financial Statement

Financial Statement for period endin 11/30/78 RECEIVED

Budget Review Committee Recommen dations

Recommendations of the Maricop County Medical Society's ArMA Budge Review Committee and progress repor of the Finance Committee RECEIVED.

Recommendation F

Response of Robert E. T. Stark, M.D Chairman, Medical Educatio Committee, dated 12/6/78 re: assumptio of processing of CME by BOME RECEIVED.

Recommendation A-1

IT WAS MOVED AND CARRIED T ACCEPT IN THEIR ENTIRETY TH RECOMMENDATIONS OF TH

ECUTIVE DIRECTOR OF THE SSOCIATION REGARDING BUD- ET PREPARATION.

e Pima Council to Immunize iozna's Children

WAS MOVED AND CARRIED TO OOPT THE RECOMMENDATION F THE FINANCE COMMITTEE HAT, WHILE THERE ARE PRESENT- Y NO FUNDS AVAILABLE FOR SUCH JRPOSE, THE REQUEST OF THE MA COUNCIL TO IMMUNIZE RIZONA'S CHILDREN BE HELD IN BEYANCE, TO BE RECONSIDERED T A TIME WHEN THE BUDGET OULD ALLOW FOR ADDITIONAL ONTRIBUTION TO DESERVING ND WORTHWHILE PROJECTS.

EDICAL EDUCATION COMMITTEE

onfirmation of Appointments

WAS MOVED AND CARRIED THAT HE APPOINTMENTS OF ALAN C. INFIELD, M.D., C. CLAYTON RIFFIN, M.D., KATHY DEASON, .D., ALEX NEWMAN, M.D., URRAY S. FELDSTEIN, M.D., DWARD F. GOLJAN, M.D., AND ERBERT M. MUNHALL, M.D., TO HE MEDICAL EDUCATION OMMITTEE FOR THE TERM 1978-80 CONFIRMED.

ccreditations Granted

ccreditations granted to Desert maritan Hospital, Phoenix Indian edical Center, Scottsdale Memorial ospital and Mesa Lutheran Hospital ECEIVED.

MA as an Accrediting Body

obert E. T. Stark, M.D., as Chairman of e Medical Education Committee, dressed the Board regarding the ntents of his letter dated November 17, 78 relative to CME accreditation and e Liaison Committee on Continuing edical Education, as well as requesting at the Board support the action taken the Medical Education Committee in meeting held September 28, 1978. Dr. ttenspiel at this point interjected rtain thoughts to the Board arising out his attendance at a reference comittee eeting concerning this matter during re recent AMA Interim Meeting in iago. Following fa lengthy discussion, WAS MOVED AND CARRIED THAT HE ARIZONA MEDICAL ASSOCIA- ION AFFIRM THE STAND ON ONTINUING MEDICAL EDUCA- ION ACCREDIATION TAKEN BY HE AMERICAN MEDICAL ASSOC- TION AT THE 1978 INTERIM EETING WHICH READS AS OLLOWS:

ESOLVED, THAT THE AMERICAN EDICAL ASSOCIATION AFFIRM HE CONCEPT OF ACCREDITATION F CONTINUING MEDICAL EDUCATION BY STATE MEDICAL ASSOCIATIONS WHOSE CONTINUING MEDICAL EDUCATION STANDARDS MEET AMERICAN MEDICAL ASSOCIATION OR LIAISON COMMITTEE ON CONTINUING MEDICAL EDUCATION (LCCME) CONTINUING MEDICAL EDUCATION STANDARDS; AND BE IT FURTHER

RESOLVED, THAT THE AMERICAN MEDICAL ASSOCIATION SEEK MODIFICATION OF THE BYLAWS OF THE LCCME TO PROVIDE FOR THE ACCREDITATION OF CONTINUING MEDICAL EDUCATION BY STATE MEDICAL ASSOCIATIONS WITH ACCREDITATION STANDARDS APPROVED BY THE AMERICAN MEDICAL ASSOCIATION CONVEY ITS SUPPORT OF THIS POLICY TO THE LCCME CONTINUING MEDICAL EDUCATION STANDARDS; AND BE IT FURTHER

RESOLVED, THAT THE AMERICAN MEDICAL ASSOCIATION SEEK MODIFICATION OF THE BYLAWS OF LCCME TO PROVIDE FOR THE ACCREDITATION OF CONTINUING MEDICAL EDUCATION BY STATE MEDICAL ASSOCIATIONS WITH ACCREDITATION STANDARDS APPROVED BY THE AMERICAN MEDICAL ASSOCIATION; AND BE IT FURTHER

RESOLVED, THAT THE AMERICAN MEDICAL ASSOCIATION CONVEY ITS SUPPORT OF THIS POLICY TO THE LCCME THROUGH ITS REPRESENTATIVE LCCME MEMBERS."

Additonally, it was the consensus of the Board that our position be forwarded to the LCCME for their information.

GOVERNMENTAL SERVICES COMMITTEE

Confirmation of Appointment

IT WAS MOVED AND CARRIED THAT THE APPOINTMENT OF DENNIS COOKRO, M.D. TO THE GOVERNMENTAL SERVICES COMMITTEE BE CONFIRMED.

STATEWIDE HEALTH COORDINATING COUNCIL

IT WAS MOVED AND CARRIED TO ACCEPT THE RECOMMENDATION OF THE GOVERNMENTAL SERVICES COMMITTEE THAT THE ARIZONA MEDICAL ASSOCIATION APPROACH THE STATEWIDE HEALTH COORDINATING COUNCIL RELATIVE TO ARMA APPOINTING A MEDICAL ADVISORY COMMITTEE TO IT.

LEGISLATIVE COMMITTEE

Confirmation of Appointment

IT WAS MOVED AND CARRIED THAT THE APPOINTMENT OF JAMES SHWAYDER, M.D. TO THE MATERNAL & CHILD HEALTH CARE COMMITTEE BE APPROVED.

Planned Parenthood Proposal

IT WAS MOVED AND CARRIED TC ACCEPT THE RECOMMENDATION OF THE MATERNAL & CHILD HEALTH CARE COMMITTEE THAT THE BOARD OF DIRECTORS TAKE NO ACTION ON THE REQUEST OF PLANNED PARENTHOOD FOR ENDORSEMENT OF THE DOCUMENT ENTITLED "PLANNED BIRTHS THE FUTURE OF THE AMERICAN FAMILY AND THE QUALITY OF AMERICAN LIFE."

PHYSICIAN REHABILITATION COMMITTEE

Assistance for BOMEX

Mr. Jacobson addressed the Board relative to the request of BOMEX to use ArMA's Physician Rehabiliation Committee and the contents of his letter dated December 12, 1978 with respect thereto No ACTION TAKEN.

PROFESSIONAL COMMITTEE

Section on Helath Education

IT WAS MOVED AND CARRIED THAT THE APPOINTMENTS OF CLARENCE R. LAING, M.D., CHARLES W. PULLEN, M.D. AND WARREN L. NICCUM, M.D. TO THE PROFESSIONAL COMMITTEE AND OF CLARENCE R. LAING, M.D. AS CHAIRMAN OF THE SECTION ON REHABILITATIVE MEDICINE, CHARLES W. PULLEN, M.D. AS CHAIRMAN OF THE SECTION ON SAFETY AND WARREN L. NICCUM, M.D. AS CHAIRMAN OF THE SECTION ON HEALTH EDUCATION BE CONFIRMED.

5th Annual Sports Medicine symposium

Program for the 5th Annual Sports Medicine Symposium, January 20 & 21, 1979 RECEIVED.

PURCHASING COMMITTEE - WPPA

Confirmation of Appointments

IT WAS MOVED AND CARRIED THAT THE APPOINTMENTS OF JOHN F. KAHLE, M.D., AS CHAIRMAN, AND OF MERRILL M. ABESHAUS, M.D., EVERETT COLBERT, ED DE VALK, LAWRENCE M. HAAS, M.D., JAMES M. HURLEY, M.D., VERNOr F. LOVETT, M.D., OLIN RAGLAND AND NEOPITO L. ROBLES, M.D., AS MEMBERS, TO THE PURCHASING COMMITTEE - WESTERN PHYSICIANS PURCHASING ASSOCIATION BE CONFIRMED.

WPPA Brochure

Western Physicians Purchasing Association borchure mailed 12/1/78. RECEIVED.

AMA DELEGATION

Reports of AMA Interim Meeting

Reports of Arthur V. Dudley, Jr., M.D.

and W. Scott Chisholm, M.D. RECEIVED.

Recommendations for Membership on AMA Councils

AMA letter of September 22, 1978 RECEIVED

State Speakers

Dr. Price briefly reported to the Board regarding a conference held during the recent AMA interim meeting relative to the conducting of business meeting and discussions of both the Sturgess and Roberts Rules of Order.

Ad Hoc Committee on a Economic Organization for Arizona Physicians

The meeting of the Ad Hoc Committee on an Economic Organization for Arizona Physicians of the Ariozna Medical Association, Inc. Held at 810 West Bethany Home Road, Phoenix, Arizona, on Saturday, January 6, 1979, convened at 12:52 p.m., Alfred F. Miller, M.D., Chairman, presiding.

FORMATION OF AN ECONOMIC ORGANIZATION FOR ARIZONA PHYSICIANS

The committee considered 1) the need for an Economic Organization for Arizona Physicians and 2) several similar type organizations presently in existence throughout the country and, following a lengthy discussion, took the following action:

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THERE BE AN ECONOMIC ORGANIZATION FOR ARIZONA PHYSICIANS AND THAT SUCH AN ORGANIZATION BE SEPARATE AND APPART FROM THE ARIZONA MEDICAL ASSOCIATION FOR THE PRUPOSE OF NEGOTIATING CONTRACTS, CARRYING ON INSURANCE GRIEVANCES FOR ITS MEMBERS, AND MONITORING THIRD PARTIES.

Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

Please consult complete prescribing information, a summary of which follows:

Indications: Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

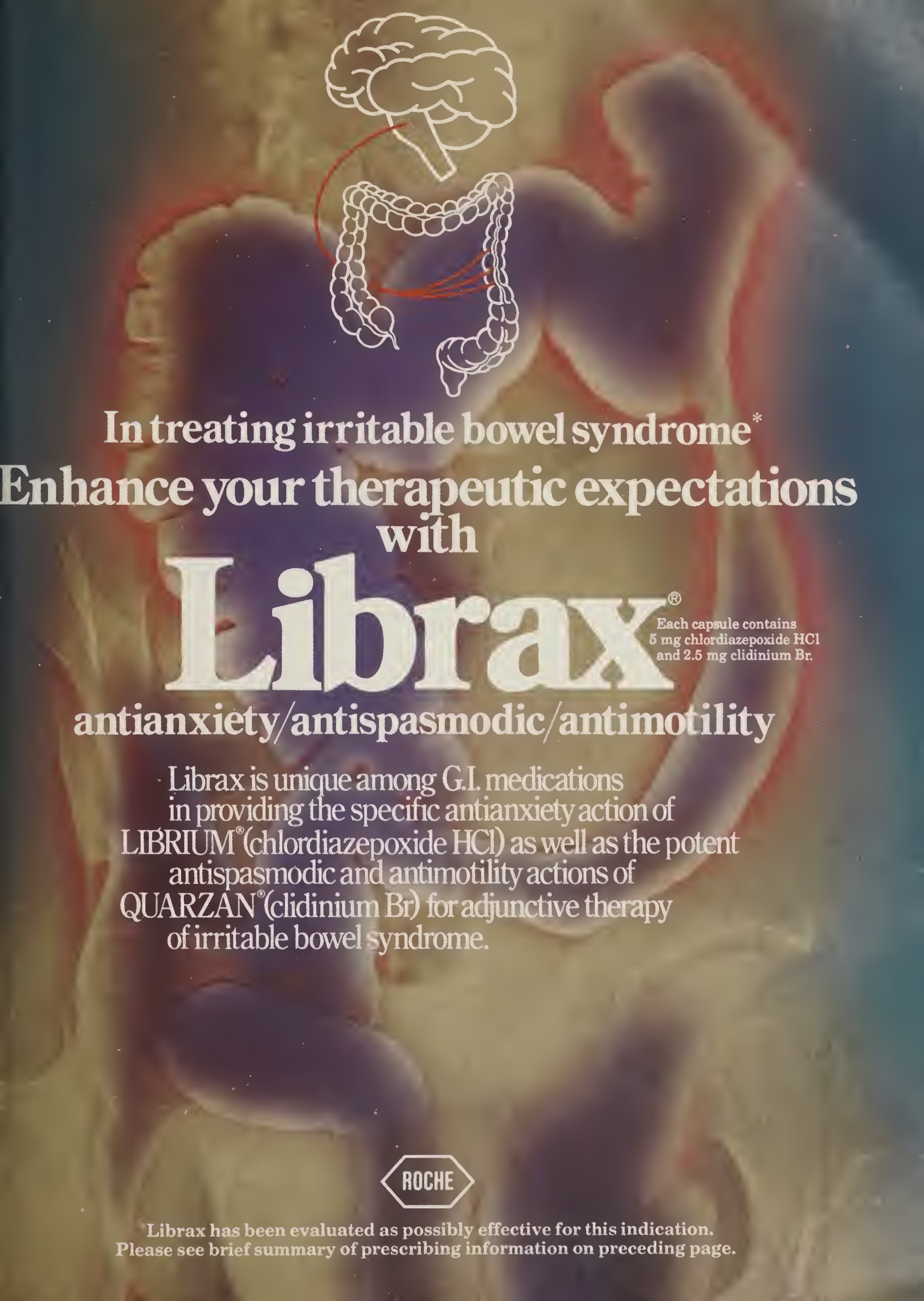
As with all anticholinergics, inhibition of lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated; avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

ROCHE

Roche Products Inc.
Manati, Puerto Rico 00701



In treating irritable bowel syndrome*

Enhance your therapeutic expectations with

Librax®

Each capsule contains
5 mg chlordiazepoxide HCl
and 2.5 mg clidinium Br.

antianxiety/antispasmodic/antimotility

Librax is unique among G.I. medications in providing the specific antianxiety action of LIBRIUM® (chlordiazepoxide HCl) as well as the potent antispasmodic and antimotility actions of QUARZAN® (clidinium Br) for adjunctive therapy of irritable bowel syndrome.

ROCHE

*Librax has been evaluated as possibly effective for this indication.
Please see brief summary of prescribing information on preceding page.

EMPIRIN® COMPOUND
c̄ CODEINE

Each tablet contains: aspirin, 227 mg; phenacetin, 162 mg; and caffeine, 32 mg; plus codeine phosphate in one of the following strengths: #4—60 mg (gr 1); #3—30 mg (gr ½); #2—15 mg (gr ¼); and #1—7.5 mg (gr ⅛), (Warning—may be habit-forming). CIII

Wellcome

Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

Future Medical Meetings

CONTINUING MEDICAL EDUCATION

The following institutions and organizations have been accredited for their continuing medical education programs by the Liaison Committee on Continuing Medical Education.

Arizona Heart Institute
Arizona Medical Association, Inc.
Arizona State Hospital, Phoenix
Desert Samaritan Hospital, Mesa
Good Samaritan Hospital, Phoenix
Health Maintenance Associates
Phoenix Indian Medical Center
Phoenix Psychiatric Council
Maricopa County General Hospital, Phoenix
Memorial Hospital, Phoenix
St. Luke's Hospital & Medical Center, Phoenix
St. Joseph's Hospital & Medical Center, Phoenix
Tucson Hospitals Medical Education Program, Tucson
U of A College of Medicine
Veterans Administration Center, Prescott
Veterans Administration Hospital, Phoenix

The accredited institutions and organizations above produce a variety of continuing medical education programs. Each accredited institution and organization is responsible for designating which of these programs meet ArMA's requirements for Category 1 credit. Physicians who participate in programs which are designated Category 1 by accredited institutions will receive Category 1 credit toward the ArMA Certificate in CME and the AMA's Physician's Recognition Award.

Advanced Cardiac Life Support Programs Instructor Course
March 23 & 24 1979. Arizona Medical Assoc., Inc., 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner at the Arizona Medical Association. Approved for 16 hours of category 1 credit.

Clinical Recognition and Management of Heart Disease — 1979
March 22,23 & 24, 1979. U of A Health Sciences Center, Main Auditorium. Sponsor: U of A College of Medicine. Contact: Registrar, American College of Physicians, 420 Pine St., Philadelphia, PA 19104.

Third Annual Southwestern Cardiovascular Symposium — 1979
March 28, 29, & 30, 1979. The Reistry Resort, Scottsdale, AZ. Sponsor: St. Luke Hospital Medical Center, 525 N. 18th St. Phoenix, AZ 85006. Contact: Public Relations, St. Luke's Hospital. Approved for 14 hours of category 1 credit.

Second International Conference on the Adjuvant Therapy of Cancer
March 28—31, 1979. Tucson Convention Center, Tucson, AZ. Sponsor: U of A College of Medicine, Cancer Center Division. Contact: Cancer Center Division, U of A College of Medicine, Tucson, AZ 85724. Approved for 23 hours of category 1 credit.

Medical History Society of Arizona
March 29, 1979, Preston T. Brown Room at Maricopa County Medical Society Building, 2025 N. Central. Contact: William C. Weese, M.D.,President at 265-0000.

Second Annual Symposium on Aging
March 31 and April 1, 1979. Sheraton-Place Hotel, San Francisco, CA Sponsor: Univ. Of California, San Francisco Schools of Medicine. Contact: Ms. Bruce, Univ. of California, San Francisco Continuing Education in Health Sciences, 1343 3rd Ave, San Francisco, CA 94143. Approved for category 1 credit.

APRIL

Fifteenth Annual Arizona Chest Symposium
April 6,7,8, 1979. Doubletree Inn, Tucson, AZ. Sponsor: College of Medicine, U of A and Tucson Medical Center. Contact: Linda Alpert, R.N., Symposium Coordinator Tucson, Medical Center, P.O. Box 6067, Tucson, AZ 85733. Approved for category 1 credit.

Management of Arthritis and Complications of the Gastrointestinal Tract
Commemorative Symposium to Honor the late David C. H. Sun, M.D.
April 14, 1979,Mountain Shadows Resort Scottsdale, Az. Sponsor: Good Samaritan Hospital. Contact: Beth Supowitz, Good Samaritan Hospital,1033 E. McDowell Rd. Approved 3 hours category 1 credit.

Fourth Annual Update: Primary Care
April 18—21, 1979, Arizona Health Sciences Center, Tucson, AZ. Sponsor: College of Medicine. Approved for category 1 credit.

88th Annual Meeting: Arizona Medical Association
April 24—28, 1979. Sponsor: Arizona Medical Association, Inc. Contact: Bruce E. Robinson, Executive Director, 810 W. Bethany Home Rd., Phoenix, Z 85014. Approved for category 1 credit.

Health Hazard Appraisal: Clinical Information for Consumer and Practitioners
April 21 & 22, 1979. Sherton-Place Hotel, San Francisco, Ca. Sponsor: University of California, San Francisco. Contact: Ms. Bruce, Univ. of California, San Francisco, Continuin Education Health Sciences, 1343 Third Ave., San Francisco, CA 94143

MAY

Update: Primary Care 1979
May 2-5, 1979, Univ. of Arizona,Arizona Health Sciences Center, 1501 N. Campbell Ave., Tucson, Az. Sponsor: Univ. of Arizona College of Medicine,Office of CME. Contact: Faith Carlisi, Conference Coordinator Office of CME,Arizona Health Sciences Center, Tucson, Az 85724. Approved for 30 hours of category 1 credit.

MONTHLY OR WEEKLY

Shrine Medics Meeting
Second Tuesday of each month, Doctors Hospital, 5:45 p.m. J. South Classroom. Sponsor: Shrine Medics. Contact: Robert C. Briggs, M.D., 5121 N. Central Ave., Phoenix, AZ 85012.

Office Psychiatry for the Primary Provider
2nd Monday of month, 4811 N. 7th Street, Phoenix, AZ. Sponsor: Arizona Health Plan. Contact: T.R. Bittker, M.D., Box 5000, Phoenix, AZ 85010. Approved for category 1 credit.

Counter Transference Group
Weekly, Thurs. 8—10 p.m. Sponsor: Phoenix Psychiatric Council. Contact. James E. Campbell, M.D., 5051 N. 34th St., Phoenix, AZ 85018. Approved for 2 hours category 1 credit.

Monthly Meeting of Tucson Radiologists
Last Tues. of month. Plaza International, Tucson, AZ. Sponsor: U of A Medical Center, Dept. of Radiology. Contact: Irwin M. Freundlich, M.D., U of A Health Sciences Center, Dept. of, Radiology, Tucson, AZ 85724. Approved for 2 hours category 1 credit.

Pediatric Grand Rounds
Tuesday 7:30-8:30 a.m in Phoenix: 1st Tues.—Phoenix Indian Hospital, 2nd Tues.—Maricopa County Hospital, 3rd Tues.—Good Samaritan Hospital, 4th Tues.—St. Joseph's Hospital. Sponsor: Maricopa County Hospital (Phoenix Hospital's Affiliated Pediatric Program). Contact: J. Kipp Charlton, M.D., 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

Review of Forensic Pathology Current Case, Special Topics
Thursday, weekly, 11 a.m., 120 S. 6th Ave., Phoenix, AZ. Sponsor: Arizona Society of Pathologists. Contact: H.H. Karnitschnig, M.D., 120 S. 6th Ave., Phoenix, AZ. Approved for 1 hour per session category 1 credit.

Staff Education Conference
Wednesdays, weekly, 1 p.m., Arizona State Hospital, Phoenix, AZ. Sponsor: Arizona State Hospital. Contact: Howard E. Wulsin, M.D., Arizona State Hospital, 2500 E. Van Buren, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

BARROW NEUROLOGICAL INSTITUTE

Medical Education
Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Sponsor: St Joseph's Hospital & Medical Center. Contact: John R. Green, M.D. Approved for 1 hour category 1 credit.

Neurology Teaching Conference
Tuesdays, 8:30-9:30 a.m., Eighth Floor Conf. Room.

Neurosurgery Morbidity Conference
Wednesdays, 8:15-9:15 a.m., on first and third weeks, Eighth Floor Conference Room.

Neuro-ophthalmology Conference
Tuesdays, 7:30 a.m. in 8th floor neurology conference room.

Spinal Injury Conference
Wednesdays, 8:15-9:15 a.m., on second and fourth weeks, in Neuropathology Conf. Rm.—a multidisciplinary review of admission by neurosurgeons, orthopedists, and rehabilitation specialists

Neuropathology of Gross Specimens Conference
Thursday, 7:30-8:30 a.m. in the Morgue.

Neurology-Neurosurgical Clinical-Neuroradiological and Neuropathological Conference
Fridays, 8-9 a.m., First Floor Conference Rm.

Neuropathology or Neuroradiology Conferences
Friday, 9 a.m., Neuropathology in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

Neurorehabilitation Conference
Tuesdays, noon, 8th Floor Conference Rm.

Neurosurgical Journal Club
Saturdays, 9-11 a.m. in Eighth Floor Conference Rm.

ogy in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

CAMELBACK HOSPITAL

5055 N. 34th St., Phoenix, AZ 85018. Sponsor: Camelback Hospital. Contact: Medical Director.

Patient Staffing Conference
Three times weekly

DESERT SAMARITAN HOSPITAL

Wednesday evenings, 7 p.m. Sponsor: Desert Samaritan Hospital. Contact: L. A. Rosati, M.D., Laboratory, Desert Samaritan Hospital, Mesa, AZ 85202. Approved for category 1 credit.

Monthly Visting Professor Program
Tuesday Evenings at 7 p.m.

Surgical Morbidity & Mortality Conference
2nd Thursday, 7 a.m., Grande Room

Department of Medicine Clinical Conferences
Thursday, 12:30—1:30 p.m., Grande Room.

OB/GYN Clinical Conferences
Monday, 12:30—1:30 p.m., Grande Room.

GOOD SAMARITAN HOSPITAL

Clinical Cancer Conference
3rd Wednesday, every month, Butler Bldg. Conference Rm. Good Samaritan Hospital. Contact: John A. Bruner, M.D., 926 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour per session category 1 credit.

Pulmonary Disease Grand Rounds
Mondays, 12 Noon, D-5 North Conf. Rm., Good Samaritan Hospital, Phoenix, AZ. Sponsor: Pulmonary Disease Teaching Service, Good Samaritan Hospital. Contact: Bernard E. Levine, M.D., Pulmonary Function Laboratory, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour category 1 credit.

MARYVALE SAMARITAN HOSPITAL

Continuing Medical Education Program
Maryvale Samaritan Hospital, every other Wednesday, 7-8 a.m., January 25, 1978

MARICOPA COUNTY GENERAL HOSPITAL

2601 E. Roosevelt, Phoenix, AZ 85008. Sponsor: Maricopa County General Hospital. Contact: H. F. Lenhardt, M.D., Dir. of Medical Education. Approved for category 1 credit.

Recent Advances in Geriatric Psychiatry
January 20, 1979. Maricopa County General Hospital

5th Annual MCGH Urological Seminar
January 27 & 28, 1979. Doubletree Inn, Scottsdale, AZ 85251.

Current Advances in Obstetrics and Gynecology
February 14, 15 & 16, 1979, Scottsdale Hilton Hotel, Scottsdale, AZ.

Medical Progress: A Review of Advances in Medicine in the Past 5 Years
Feb. 22, 23 &, 24, 1979. Carefree Inn, Carefree, AZ 85331.

The Head
Presented by Dept. of Radiology, Feb. 9, 10 11, 1979. Doubletree Inn, Scottsdale, AZ 85251

MEMORIAL HOSPITAL

1201 S. 7th Ave., Phoenix, AZ 85036. Sponsor: Memorial Hospital. Approved for category 1 credit.

Month Medical Education Seminar
Third Monday, 6:30 p.m., Kiva Conference Rm. Contact: George Scharf, M.D.

Tumor Board Conference
Every Friday at Noon, Kiva Conference Rm. Contact: Howard Kimball, M.D.

SCOTTSDALE MEMORIAL HOSPITAL

7300 E. 4th St., Scottsdale, AZ 85251. Sponsor: Scottsdale Memorial Hospital. Contact: W. S. Wlliams, M.D., Director of Medical Education

Clinical Pathological Conference
4th Monday, monthly, 12:45 p.m.

Family Practice Conference
1st Monday, monthly, 12:45 p.m.

Medical Grand Rounds
3rd Monday, monthly, 12:45 p.m.

Morbidity & Mortality Conference
2nd Monday, monthly, 12:45 p.m.

ST MARY'S HOSPITAL & HEALTH CENTER

1601 W. St. Mary's Rd., Tucson, AZ 85703 Sponsor: St. Mary's Hospital & Health Center Contact: see below.

Cardiology Conference
Every Friday 8-9 a.m., Century Rm. A Contact: Anthony L. Forte, M.D. Approved for category 1 credit.

Monthly Specialty Conference of the Department of Surgery
First Monday, monthly, 7:30 a.m. Centur Rm. A. Contact: Medical Staff Office Approved for 1 hour of category 1 credit

Grand Rounds: Medical Surgical, Family Practice, Pathology, Radiology
Weekly, Thursday, 7-8:30 a.m. Contact Richard A. Silver, M.D. Approved for 1 hour of category 1 credit.

U OF A HEALTH SCIENCES CENTER

Sponsor: U of A College of Medicine, Tucso AZ 85724. Contact: See below. Approved f category 1 credit.

Clinical Immunology, Allergy & Rheumatology Rounds
Every Friday, Noon-1 p.m. Contact: Joh Boyer, M.D., Dept. of Internal Medicine.

Cerebrovascular Disease Conference
Mondays, 5-6 p.m., weekly, Rm. 550 Contact: Wesly Moore, M.D.,Depts. Surgery, Nurology & Radiology.

Dean's Clinical Rounds
October 18, 1978, Main Auditorium, UAHS Contact: Louis J. Kettel, M.D.

Endocrinology Seminar
Every Thursday, Noon-1 p.m., 1st, 3rd & 5t Thursday, Room N318, VA Hospital. 2nd 4th Thursday, Room 6505, Tucson Medic Center. Contact: Dept. of Internal Medicin

Hematology-Oncology Clinical Conferenc
Every Tuesday, Noon-1 p.m., 1st, 3rd & 5t Tuesdays, Rm 6505, Tucson Medical Cente 2nd & 4th Tuesdays, Rm. N318, VA Hospita Contact: Sidney Salmon, M.D., Dept. Internal Medicine.

Joint Thyroid Clinic Conference
1st & 3rd Wednesdays of every month. AHS Rm. 6505. Contact: Sidney Werner, M.D Dept. of Internal Medicine, Endocrinolo Section.

Medical Grand Rounds
Every Wed., Noon-1p.m., 1st, 3rd, & 5th We Staff Conf. Room, VA Hospital. 2nd & 4 Wed.,Rm. 5403, UAHSC. Contact: Jay Smit M.D., Dept. of Internal Medicine.

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ROBERT S. WALDMAN, M.D.

uclear Medicine
hursday, 7:30 a.m., Radiology Conf. Rm., AHSC. Contact: Irwin M. Freundlich, M.D., ept. of Diagnostic Radiology.

eurology Grand Rounds
Every Friday, Noon, 1st, 3rd, & 5th Fridays, AHSC, Rm. 7505. 2nd & 4th Fridays, VA ospital. Contact: William A. Sibley, M.D., ept. of Neurology.

europathology Review Conference
hursdays, 8:30 a.m., Rm. 5120, UAHSC. ontact: Peter C. Johnson, M.D.

eurosciences Seminar
very Friday, 7:30 a.m.,UAHSC, Rm 7505. ontact: Colin R. Bamford, M.D., or Jose F. aguna, M.D., Dept. of Neurology.

athology Seminar
riday, 4:30-5:30 p.m., Rm. 5120, UAHSC. ontact: Paul Finley, M.D., Dept. of athology.

ucson Pathologist Conference
irst Monday of the Month, 7:30-9 p.m. otation between Tucson Pathology Conf. ms. Contact: Anna Graham, M.D., Tucson athologists.

ediatric Grand Rounds
very Tuesday, 12:30-1:30 p.m. Alternates etween Tucson Medical Center & UAHSC. ontact: Hugh Thompson, M.D., Dept. of ediatrics.

Problem Case Workshop
3rd Monday of each month, 7:30 a.m., Rm 4410, UAHSC. Contact: H. E. Cross, M.D., Ph.D., Div. Of Ophthalmology.

Psychiatric Grand Rounds
Every Wednesday, Sept. to May 4, 5:30 p.m., Rm8403 UAHSC. Contact: Alan Levenson, M.D., Dept. of Psychiatry.

Chest Radiology
Monday, 5-6 p.m., weekly, Rm 1535F, UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Gastrointestinal Radiology
Mondays, 7:30 a.m., weekly except for summer months. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Radiation Oncology Planning Conference
Friday, weekly, 8:30-10 a.m., UAHSC, Rm. 0655. Contact: Robert S. Heusinkveld, M.D., Radiation Oncology Section.

Radiology-Rheumatology Conference
Thursday, 8 a.m., UAHSC, Library Rm.1535C. Contact: Irwin M. Freundlich, M.D. Dept. of Radiology.

Vascular Radiology
Radiology Interesting Case Conference
Thursday, Noon, VA Hospital. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Resident's Conference
Wednesday, weekly 5-6 p.m., Diag. Radiology Conf. Rm. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology

Trauma Conference
Every Thursday,4-5 p.m. UAHSC, Rm. 5505. Contact: Martin Silverstein, M.D., Dept. of Surgery.

Grand Ward Rounds—Trauma
Every Tuesday, 8 a.m., UAHSC. Contact: Martin Silverstein, Surgery Dept., Trauma Section.

Monthly Meeting Tucson
Ultrasonography Group
First Wed. of month, 4:30-5:30 p.m., UAHSC. Contact: Irwin M. Freundlich, M.D.

Tucson Urological Society
Scientific Meeting
Monthly. Contact: George W. Drach, M.D., Depts. of Surgery & Urology.

General Urology Conference
Tuesday 5-6 p.m. Thursday, Noon-1:30 p.m. UAHSC Meeting Rooms & VA Hospital. Contact: George W. Drach, M.D., Dept of Surgery/Urology Section.

VETERANS ADMINISTRATION HOSPITAL

7th St. and Indian School Rd., Phoenix, AZ 85012. Sponsor: VA Hospital. Contact: Jasper L. McPhail, M.D. Approved for Category 1 credit.

Academic Surgery Conference
Each Thursday — 2 p.m. — C435, Dr. Cannon, Ext. 493.

Cardiology Conference
2nd Thursday — 1 p.m. — T5, Dr. Habibzadeh, Ext. 348.

Cancer Symposium
Each Wednesday — 1 p.m. — T5, Dr. Berkley, Ext. 419.

Clinical Conference
4th Thursday of 3rd Month, (Mar. Jun., Sept., & Dec.), 1 p.m. — T5, Dr. Likos, Ext. 623.

Dermatology Conference
1st, 2nd, & 3rd Wednesday (usually, but is subject to change) 10 a.m. — C118, Dr. Roberts, Ext. 426.

G.I. Radiology Clinical Correlation Conference 1st & 3rd Monday — 1 p.m. — C435, Dr. Sanowski, Ext. 618.

G.I. Grand Rounds
Ech Tuesday — 1 p.m. — T5, (4th Thursday with U of A Consultants) Dr. Sanowski, Ext. 618.

Medical Service Grand Rounds
Each Friday — 11 a.m. — T5, Dr. Zeller, Ext 272

Medical-Surgical Chest Conference
1st and 3rd Thursday — 1 p.m. — T5, Dr. Chowdhury, Ext. 388.

Medical-Surgical G.I. Conference
Ist & 3rd Friday — 2 p.m. — 2123, Dr. Sanowski, Ext. 618.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery-Pathology Conference
Each Thursday — 2 p.m. — 2128, Dr. Cannon, Ext 493, & Dr. Likos, Ext. 623.

Urology-Pathology Conference
Each Wednesday — 7 a.m. — 2128, Dr. Likos, Ext. 623 & Dr. Pentenney, Ext., 417.

ArMA 88th Annual Meeting
April 25—29, 1979
Safari Resort, Scottsdale

NEW DIRECTIONS

Wednesday April 25
Board of Directors Meeting — 8 a.m.
House of Delegates Meeting 1st General Session — 10 a.m.
Reference Committee Meetings — 2 p.m.

Thursday April 26
"Physicians Families" - Special Program 2 p.m.
Annual Golf Tournament — 12 noon
Annual Tennis Tournament — l p.m.
5th Annual National Calliope Concert — 6 p.m.
Reception and Steak Fry — 7 p.m.

FRIDAY APRIL 27
House of Delegates 2nd General Session — 8 a.m.
Scientific Program begins — 2 p.m.
ArMPAC Reception and Banquet — 7 p.m.

Saturday April 28
Breakfast Panel — 7 a.m.
Scientific Program Resumes — 9 a.m.
President's Reception and Banquet — 7 p.m.

Sunday April 29
Breakfast Panel — 7 a.m.
Scientific Program Resumes — 9 a.m.
Meeting concludes — 12 noon

CARDIOVASCULAR NUCLEAR MEDICINE UPDATE:

INDICATIONS & TECHNIQUES

PRESENTED BY
ARIZONA HEART INSTITUTE
and
SCRIPPS CLINIC & RESEARCH
FOUNDATIONS

Saturday, May 12, 1979
Marriott's Camelback Inn
Scottsdale, Arizona

PURPOSE

Radioisotopic studies are one of the fastest growing areas of cardiovascular medicine, providing an accurate and important form of noninvasive diagnosis The latest techniques used in myocardial perfusion imaging gated wall motion studies, and pyrophosphate acute myocardial infarct imaging will be presented by a distinguished faculty of leading nuclear medicine specialists Among the topics addressed in this one-day seminar will be indications for scanning in asymptomatic patients, comparisons of individual stress ECG tests with stress tests combined with nuclear scanning correlation of scintigraphy with coronary arteriography, and the role of nuclear medicine in the evaluation of postsurgical patients

This program, directed toward the practical application of nuclear diagnosis in cardiovascular medicine, will be of benefit to cardiologists, internists, family physicians, radiologists, nuclear medicine specialists, and other specialty groups interested in a state-of-the-art discussion of nuclear diagnostics in cardiovascular medicine

ACCREDITATION

This continuing medical education activity meets the criteria for 6 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association, and is acceptable for 6 Elective hours by the American Academy of Family Physicians

REGISTRATION

Registration Fee $100
Residents, Technicians, and Nurses $50

Registration Fee includes lunch

8 30	Which Noninvasive Test and When? Applying Serial Bayesian Analysis	Daniel S Berman, M D
	Stress Radionuclide Ventriculography to Detect Coronary Artery Disease	William L Ashburn, M D
9 50	BREAK	
10 20	Hot Spot Myocardial Infarct Imaging	James T Willerson, M D
	Practical Application of Thallium-201 Scintigraphy in the Coronary Care Unit	Frans J. Th Wackers, M D
11 45	LUNCH	
1 15	Assessing Acute Myocardial Infarction by Equilibrium Blood Pool Scintigraphy	Daniel S Berman, M D
	Sizing Acute Myocardial Infarcts Scintigraphically	James T Willerson, M D
2 35	BREAK	
3 05	Pitfalls in Reading Thallium-201 Images	Frans J Th Wackers, M D
	"First Pass" & "Equilibrium" Radionuclide Angiography— Methods & Applications	William L Ashburn, M D
4 25	What Can You and Your Patients Expect From Nuclear Cardiology	Panel Drs. Ashburn, Berman Wackers, & Willerson

FACULTY

William L. Ashburn, M.D.
Division of Nuclear Medicine
University of California San Diego
San Diego, CA

Daniel S Berman, M.D.
Department of Nuclear Medicine
Cedars-Sinai Medical Center
Los Angeles, CA

Frans J. Th. Wackers, M.D.
Section of Cardiology
Yale University School of Medicine
New Haven, CT

James T. Willerson, M.D.
Division of Cardiology
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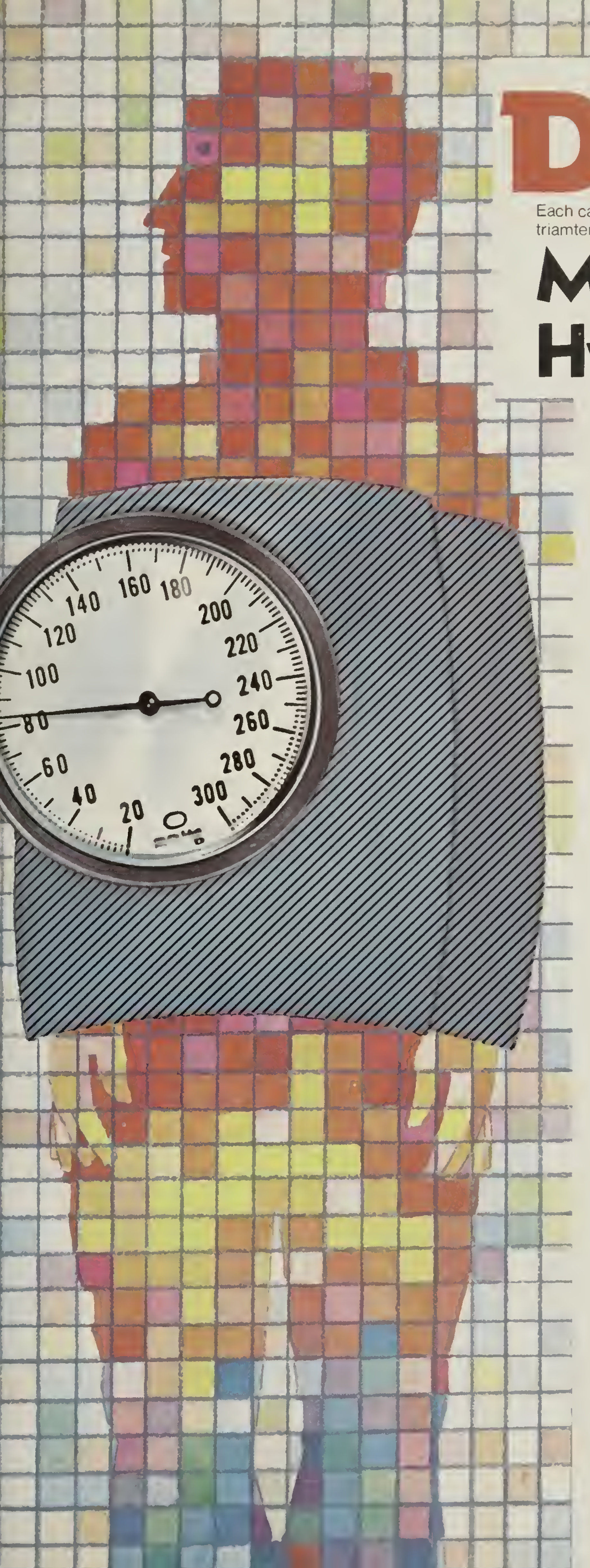

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Each capsule contains 50 mg. of Dyrenium® (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Makes Sense in Hypertension*

Before prescribing, see complete prescribing information in SK&F Co. literature or *PDR*. A brief summary follows:

* Warning
This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K+ frequently; both can cause K+ retention and elevated serum K+. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth, anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions, nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

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When painful spasm is the presenting symptom . . .

.in the functional bowel/irritable bowel syndrome*

Bentyl®

(dicyclomine hydrochloride USP)

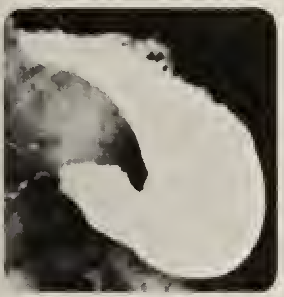
10 mg. capsules, 20 mg. tablets,
10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity with minimal anticholinergic side effects†

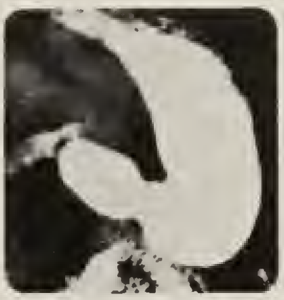
Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:
King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

Merrell

8-4420 (Y736A) MNR-804

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(dicyclomine hydrochloride USP)

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Brief Summary

INDICATIONS
Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective:

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS. Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient; unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. WARNINGS: In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. PRECAUTIONS: Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with. Autonomic neuropathy Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur ADVERSE REACTIONS: Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia, increased ocular tension; loss of taste, headache; nervousness; drowsiness; weakness; dizziness; insomnia, nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. DOSAGE AND ADMINISTRATION Dosage must be adjusted to individual patient's needs.

Usual Dosage Bentyl 10 mg capsule and syrup: *Adults:* 1 or 2 capsules or teaspoonfuls syrup three or four times daily *Children.* 1 capsule or teaspoonful syrup three or four times daily *Infants:* ½ teaspoonful syrup three or four times daily (May be diluted with equal volume of water.) Bentyl 20 mg.: *Adults* 1 tablet three or four times daily. Bentyl Injection: *Adults* 2 ml (20 mg.) every four to six hours intramuscularly only. NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE: The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.

Product Information as of October, 1978.

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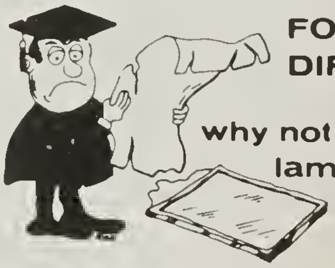

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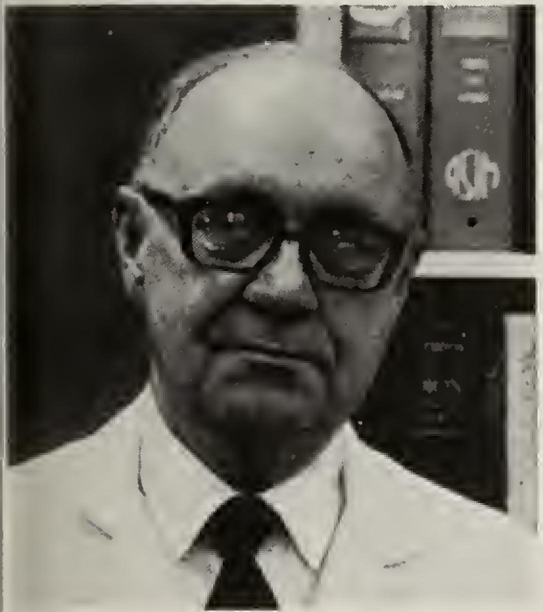

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*PATIENT CARE Magazine—Outlook 1977, "Face-Off: Cost Containment vs. Chaos," January 1, 1977.

Lyle CB, et al. "Practice habits in a group of eight internists," ANNALS OF INTERNAL MEDICINE 84 (May 1976), 594-601.

Schroeder SA, et al. "Use of laboratory tests and pharmaceuticals: variation among physicians and effect of cost audit on subsequent use," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 225 (Aug. 20, 1973), 969-73.

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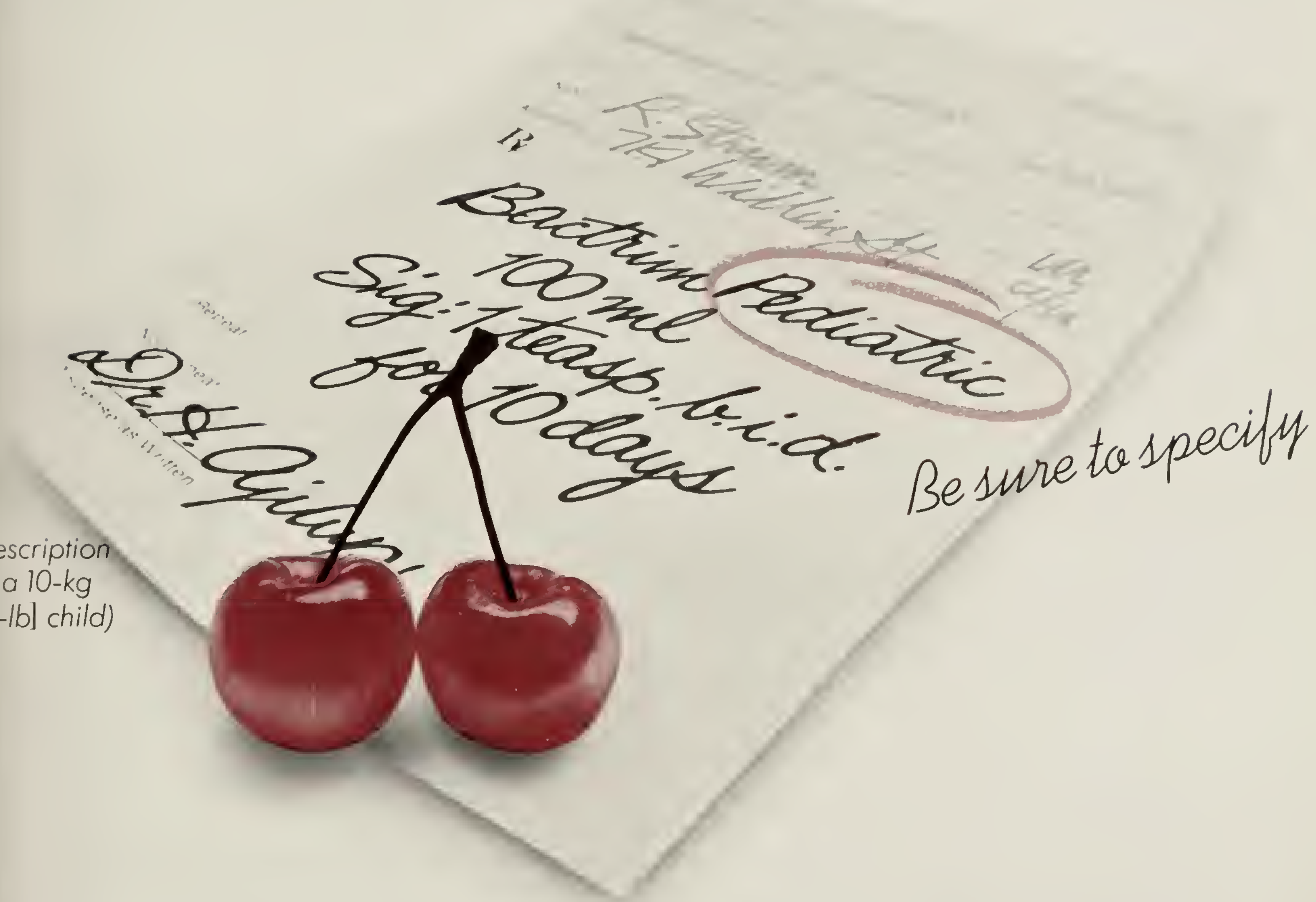

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Children Recommended dosage for children with urinary tract infections or acute otitis media—8 mg kg trimethoprim and 40 mg kg sulfamethoxazole per 24 hours in two divided doses for 10 days Use identical daily dosage for 5 days for shigellosis A guide follows
Children two months of age or older

Weight		Dose – every 12 hours	
lbs	kgs	Teaspoonfuls	Tablets
22	10	1 teasp (5 ml)	½ tablet
44	20	2 teasp (10 ml)	1 tablet
66	30	3 teasp (15 ml)	1½ tablets
88	40	4 teasp (20 ml)	2 tablets or 1 DS tablet

For patients with renal impairment

Creatinine Clearance (ml min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	½ the usual regimen
Below 15	Use not recommended

PNEUMOCYSTIS CARINII PNEUMONITIS Recommended dosage 20 mg kg trimethoprim and 100 mg kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days See complete product information for suggested childrens dosage table
Supplied: *Double Strength (DS) tablets* each containing 160 mg trimethoprim and 800 mg sulfamethoxazole bottles of 100 Tel-E Dose* packages of 100 Prescription Paks of 20 *Tablets*, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500, Tel-E Dose* packages of 100 Prescription Paks of 40, available singly and in trays of 10 *Pediatric Suspension*, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole cherry flavored—bottles of 16 oz (1 pint) *Suspension*, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole fruit-licorice flavored bottles of 16 oz (1 pint)

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April, 1979 Meetings

April 4–7	**Tennessee Medical Association** Airport Milton Inn Memphis, Tennessee
April 19–21	**Alabama Medical Association** Birmingham Hyatt House, Civic Cente Birmingham, Alabama
April 19–22	**Missouri State Medical Association** Chase-Park Plaza Hotel St. Louis, Missouri
April 20–22	**Georgia Medical Association** De Soto Hilton Savannah, Georgia
April 21–22	**Iowa Medical Society** Hyatt House Des Moines, Iowa
April 22–25	**Arkansas Medical Society** Little Rock Convention Center Little Rock, Arkansas
April 25–29	**Arizona Medical Association** Safari Hotel Scottsdale, Arizona
April 26–29	**South Carolina Medical Association** Myrtle Beach Hilton Myrtle Beach, South Carolina
April 29– May 2	**Nebraska Medical Association** Holiday Inn Kearney, Nebraska

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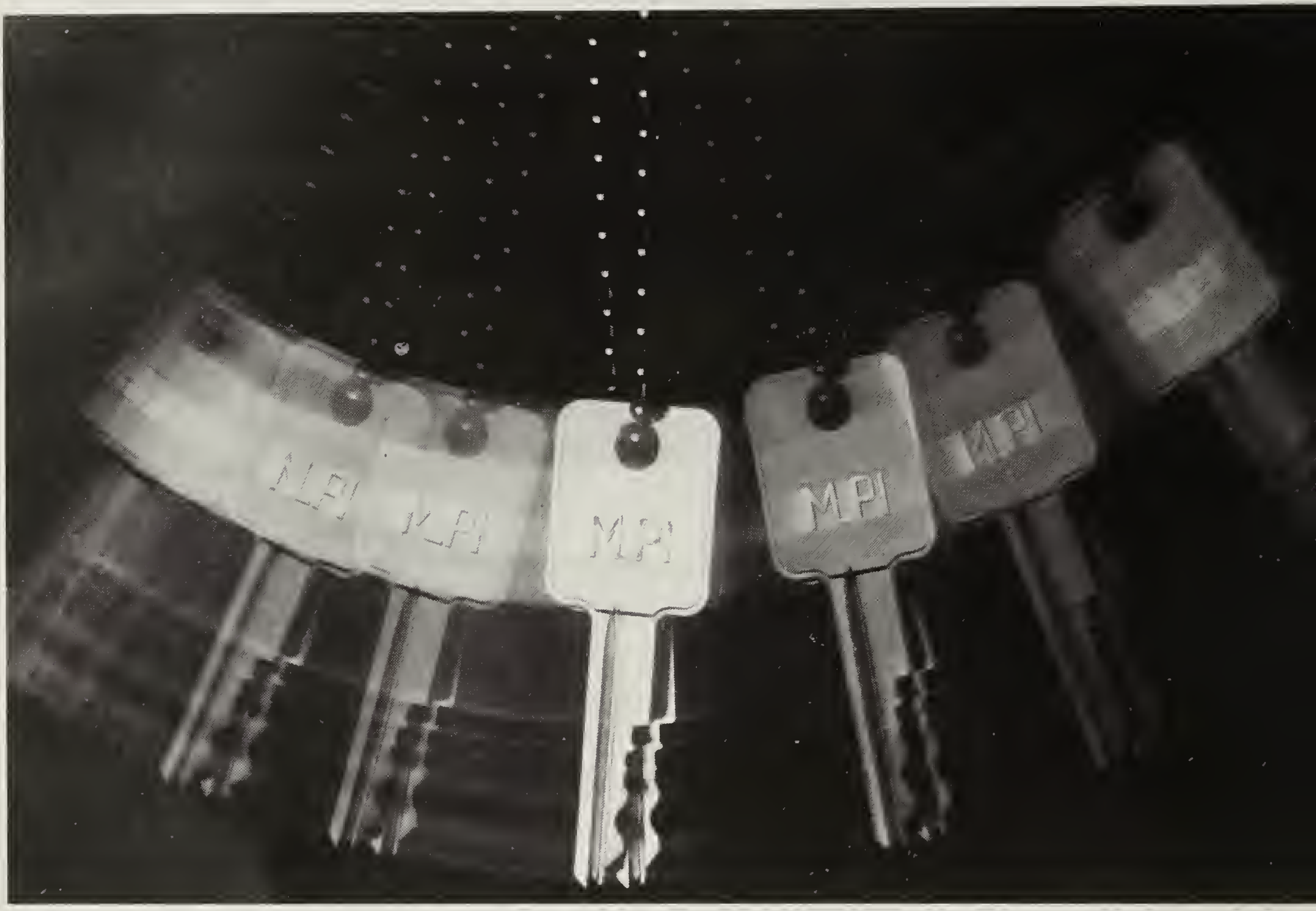

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ArMA 88th Annual Meeting
April 25—29, 1979
Safari Resort, Scottsdale

NEW DIRECTIONS

Wednesday April 25

Board of Directors Meeting — 8 a.m.

House of Delegates Meeting 1st General Session — 10 a.m.

Reference Committee Meetings — 2 p.m.

Thursday April 26

"Physicians Families" - Special Program 2 p.m.

Annual Golf Tournament — 12 noon

Annual Tennis Tournament — I p.m.

5th Annual National Calliope Concert — 6 p.m.

Reception and Steak Fry — 7 p.m.

FRIDAY APRIL 27

House of Delegates 2nd General Session — 8 a.m.

Scientific Program begins — 2 p.m.

ArMPAC Reception and Banquet — 7 p.m.

Saturday April 28

Breakfast Panel — 7 a.m.

Scientific Program Resumes — 9 a.m.

President's Reception and Banquet — 7 p.m.

Sunday April 29

Breakfast Panel — 7 a.m.

Scientific Program Resumes — 9 a.m.

Meeting concludes — 12 noon

Tenuate® Ⓒ
(diethylpropion hydrochloride NF)

Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence:* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
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Direct Medical Inquiries to
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Cincinnati, Ohio 45215, U.S.A.

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References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon, R H., and Leyland, H.M.: A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy, Jan. 20-21, 1977.

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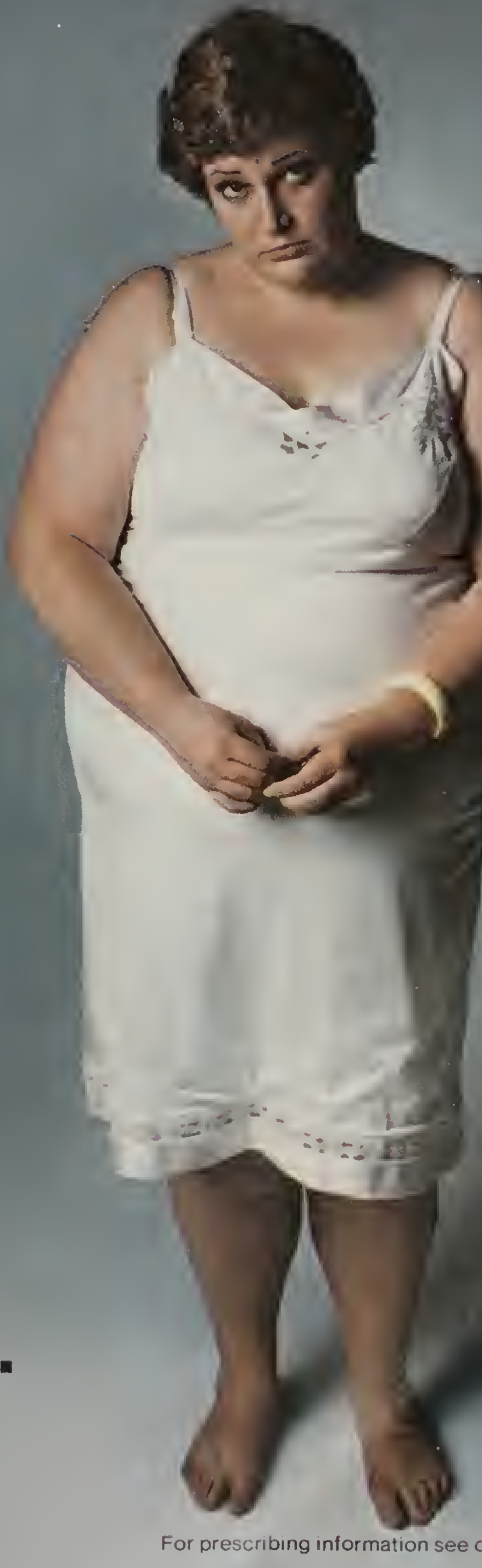
(diethylpropion hydrochloride NF)

75 mg. controlled-release tablets



A useful short-term adjunct in an indicated weight loss program.

Overweight patients in certain diagnostic categories often require strict obesity control. Diethylpropion hydrochloride has been reported useful in obese patients with hypertension, symptomatic cardiovascular disease, or diabetes. While it is not suggested that Tenuate in any way reduces these complications in the overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. (Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.)

In uncomplicated obesity.

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

Clinical effectiveness.

The anorexic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.[1] And the unique chemistry of Tenuate provides "...anorexic potency with minimal overt central nervous system or cardiovascular stimulation."[2] Compared with the amphetamines, diethylpropion has minimal potential for abuse.

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For prescribing information see opposite page

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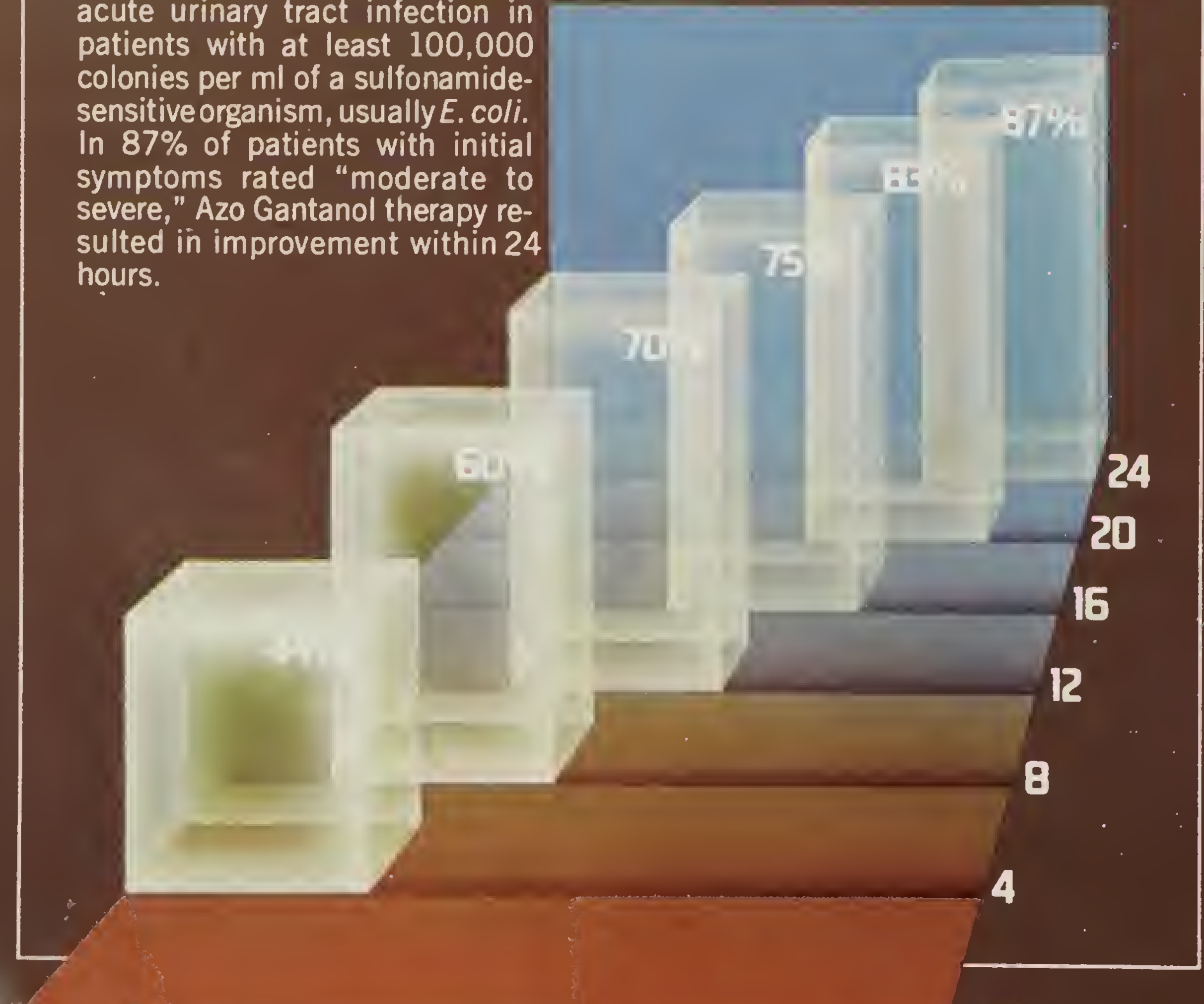

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for
the pain

for
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*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110.

Before prescribing, please consult complete
uct information, a summary of which follows
Indications: In adults, urinary tract infection
complicated by pain (primarily pyelonephriti
pyelitis and cystitis) due to susceptible orga
(usually *E. coli*, *Klebsiella-Aerobacter*, *Stap*
coccus aureus, *Proteus mirabilis*, and, less f
quently, *Proteus vulgaris*) in the absence of
obstructive uropathy or foreign bodies. **Note**
fully coordinate *in vitro* **sulfonamide sensitiv**
tests with bacteriologic and clinical respons
aminobenzoic acid to follow-up culture medi
Increasing frequency of resistant organisms
the usefulness of antibacterials including su
fonamides. Measure sulfonamide blood level
variations may occur; 20 mg/100 ml should
maximum total level.
Contraindications: Children below age 12; su
fonamide hypersensitivity; pregnancy at term
during nursing period; because Azo Gantano
tains phenazopyridine hydrochloride it is co
dicated in glomerulonephritis, severe hepati
uremia, and pyelonephritis of pregnancy wit
disturbances.
Warnings: Safety during pregnancy not estab
Deaths from hypersensitivity reactions, agra
tosis, aplastic anemia and other blood dyscr
have been reported and early clinical signs (
throat, fever, pallor, purpura or jaundice) ma
dicate serious blood disorders. Frequent CB
urinalysis with microscopic examination are
ommended during sulfonamide therapy.
Precautions: Use cautiously in patients with
paired renal or hepatic function, severe aller
bronchial asthma; in glucose-6-phosphate
dehydrogenase-deficient individuals in whom
dose-related hemolysis may occur. Maintain
adequate fluid intake to prevent crystalluria
stone formation.
Adverse Reactions: *Blood dyscrasias* (agran-
ulocytosis, aplastic anemia, thrombocytope
leukopenia, hemolytic anemia, purpura, hyp
thrombinemia and methemoglobinemia); *all*
reactions (erythema multiforme, skin erupti
Stevens-Johnson syndrome, epidermal necr
urticaria, serum sickness, pruritus, exfoliati
dermatitis, anaphylactoid reactions, periorbi
edema, conjunctival and scleral injection, p
sensitization, arthralgia and allergic myocar
G.I. reactions (nausea, emesis, abdominal p
hepatitis, diarrhea, anorexia, pancreatitis an
stomatitis); *CNS reactions* (headache, perip
neuritis, mental depression, convulsions, at
hallucinations, tinnitus, vertigo and insomni
miscellaneous reactions (drug fever, chills, t
nephrosis with oliguria and anuria, periarter
nodosa and L. E. phenomenon). Due to cert
chemical similarities with some goitrogens,
uretics (acetazolamide, thiazides) and oral h
glycemic agents, sulfonamides have caused
instances of goiter production, diuresis and
glycemia. Cross-sensitivity with these agents
exist.
Dosage: Azo Gantanol is intended for the ac
painful phase of urinary tract infections. *Usu*
adult dosage: 2 Gm (4 tabs) initially, then 1
(2 tabs) B.I.D. for up to 3 days. If pain persi
causes other than infection should be sough
After relief of pain has been obtained, conti
treatment with Gantanol (sulfamethoxazole)
be considered.
NOTE: Patients should be told that the oran
dye (phenazopyridine HCl) will color the urin
Supplied: Tablets, red, film-coated, each co
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phenazopyridine HCl—bottles of 100 and 50

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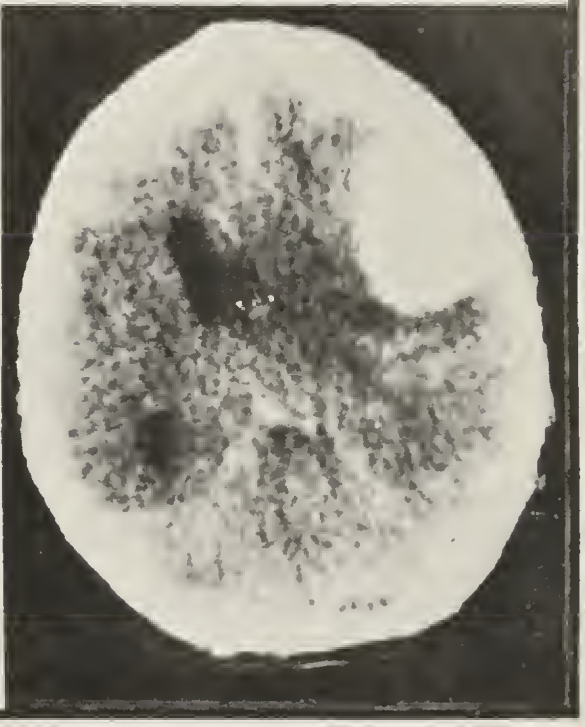

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THE CHICAGO DEPARTMENT OF HEALTH

NEWS LETTER

VOL. 18, NO. 1, MAY, 1978

AUTOMATIC BLOOD PRESSURE DEVICES

A Chicago Department of Health report on the Vita-Stat automated blood pressure machines concludes that their consistency and accuracy is sufficient for screening purposes.

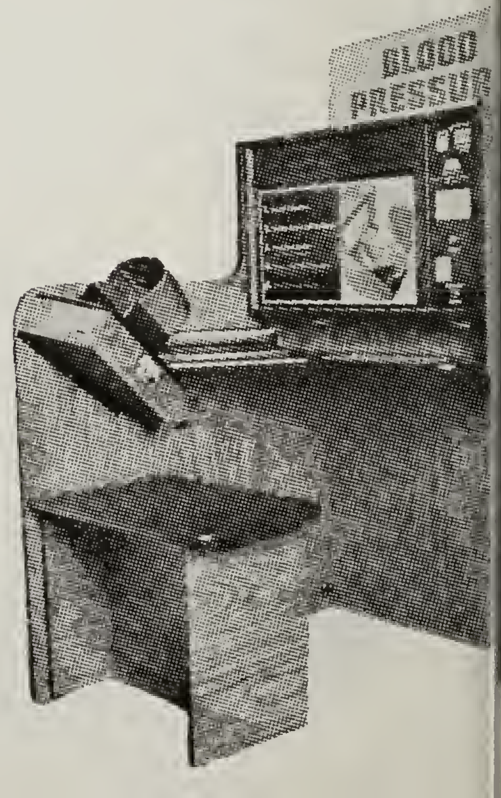
The report, the first in the nation based on a scientific study by a public agency, was prepared under the direction of Dr. David M. Berkson, the Department's heart disease control officer. It consists of (1) a statistical evaluation by Drs. Shekelle and Raynor of Rush-Presbyterian St. Luke's Medical Center, based on data collected over a four month period by Lawrence Shireman and Thomas Whipple and their co-workers in the Health Department, and (2) an evaluation of the results with recommendations for regulatory actions if deemed necessary. The report notes at the outset that any assessment of automatic blood pressure devices must compare their measurements with measurements by trained observers recorded by the traditional cuff ausculatory method. Since blood pressure may vary rapidly, the assessment of accuracy of measurement is difficult.

"In our evaluation of the Vita-Stat machine," the report states, "we found that, when the machine and a trained observer measure blood pressure simultaneously, there is a very good agreement." It is essential, however, that a machine must perform well in sequential measurement with trained observers as well as in simultaneous measurement. In sequential measurement the machine, in general, has a fair degree of accuracy. It does not perform as well, however, as trained technicians. In the laboratory analysis of the comparison between one machine and several technicians the machine tended to read systolic pressure 3.4mm higher and diastolic pressure 2.3mm lower. In the field analysis the machine tended to read systolic blood pressure 1.5mm and diastolic pressure 0.5mm higher than the technicians.

Although agreement between technicians in mean blood pressure measurement and in categorizing persons as normal, borderline or hypertensive tends to be closer than technician-machine agreement, these differences are small and of little practical significance in screening.

The report recommends that if licensing is insituted by the City of Chicago, periodic recalibration and testing should be required. The public must be informe that these instruments serve merely screening devices; that they do not repla medical consultation and that, becau blood pressure is subject to variatio several elevations or lack of elevations not constitute a diagnosis of hypertensio or normotension.

Blood pressure readings must interpreted by a qualified medical profe sional and self-adjustment of medicatio based on automated blood pressure rea ings without medical supervision may dangerous. The report concludes "th although the Vita-Stat machine does n perform as well as trained technicians, i consistency and accuracy is sufficient f screening purposes."



Seminars in Chest Medicine

he Adult Respiratory istress Syndrome

red Hosler, M.D.
Villiam C. Weese, M.D.

The rapid and inexorably progressive development of spiratory failure (RF) is a feature of many systemic as ell as localized pulmonary disorders. RF may occur in eviously healthy individuals or in the face of chronic rdiopulmonary disease.[1] While clinical, pathological, d physiological pictures are similar and felt to be due diffuse injury to the lung, etiologies are protean.

Rapidly progressive RF has been long recognized since s initial description during the influenza pandemic of 918-1919.[2] During World War I, its association with aumatic shock was called "massive collapse of the ng," while during World War II "wet lung syndrome" as used to describe the post-traumatic respiratory sufficiency.[3] In 1950, the entity of "congestive electasis" was attributed to fluid overload. dditionally, prior to 1940, intractable RF had been escribed in association with drowning, central nervous stem injury, inhalation of toxic gases, and fat nbolism.[2,4] All these clinical descriptions have now een categorized into an entity called the adult spiratory distress syndrome (ARDS).

With so wide a spectrum, ARDS is actually a ndrome rather than a specific disease. Indeed, some thors have suggested that the term ARDS be scarded and the specific etiologies be more strongly nphasized.[5] Due to the multitude of associated nditions, the exact incidence of ARDS is unknown; owever, it was estimated to afflict approximately 50,000 patients in 1972.

The etiology of ARDS is unknown; it probably presents the final common pathway of various lmonary insults. Despite the wide spectrum of recipitating factors, clinical presentation is remarkable nstant with four basic features: 1) respiratory istress, 2) hypoxemia, 3) decreasing compliance or increasing "stiffness" of the lungs, and 4) diffuse pulmonary infiltrates on chest roentgenogram. Pathologic states associated with the development of ARDS are innumerated in Table 1.

Table 1
Etiology of the Adult Respiratory Distress Syndrome

1. Shock of any etiology
2. Infectious casuses
    - Gram-negative sepsis
    - Viral pneumonia
    - Bacterial pneumonia
3. Trauma
    - Fat emboli
    - Lung contusion
    - Central nervous system trauma
4. Liquid aspiration
    - Gastric contents
    - Drowning (fresh or salt water)
    - Hydrocarbon ingestion
5. Drug overdosage
6. Inhalation of toxic gases
    - High concentration of oxygen
    - Smoke
    - Corrosive chemicals (i.e. NO , CL , NH , phosgene, cadmium)
7. Hematologic disorders
    - Intravascular coagulation
    - Post blood transfusion
    - Post percardiopulmonary bypass
8. Metabolic disorders
    - Pancreatitis
    - Uremia
    - Paraquat ingestion
9. Miscellaneous causes
    - Lymphantitic carcinomatosis
    - Increased intracranial pressure
    - Eclampsia
    - Post-cardioversion
    - Radiation pneumonitis

Common to all these underlying disorders appears to be damage to the alveolar-capillary membrane. In some cases (i.e. viral pneumonia, fat embolism, inhalation of toxic substances such as oxygen and corrosive chemicals), etiology of the injury is well understood; in others, such an increased permeability has been postulated.

As a result of injury, alveolar-capillary integrity is disrupted, leading to development of interstitial and alveolar edema. According to the Starling equation, the flux of fluid from the capillary lumen to the interstitial space is normally controlled by two forces; hydrostatic pressure and oncotic pressure. This flux normally is directed from the capillary lumen to the interstitial space, with pulmonary lymphatics removing the excess fluid.

In pulmonary edema of cardiac origin,the major precipitating force is the increased capillary hydrostatic pressure; this is reflected by an increased pulmonary arterial wedge pressure. The integrity of the alveolar-capillary membrane remains intact, and the protein

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om: St. Joseph's Hospital and Medical Center, Phoenix, AZ 85013, r. Hosler). 550 West Thomas Rd., Phoenix, AZ 85013, (Dr Weese).

content of the alveolar fluid is 30-40% that of plasma protein.[2] By contrast, in ARDS, there is a leak of high molecular weight substances across a damaged alveolar-capillary membrane; in this instance, the protein content of edema fluid approximates that of the plasma.[2] Damage to the alveolar-capillary membrane (as reflected by increased permeability) can rapidly result in an increase in total lung water content without any appreciable increase in the hydrostatic or oncotic pressures.

In cardiogenic pulmonary edema with an intact alveolar-capillary membrane, the oncotic gradient between the capillary lumen and the interstitial space is accentuated, thereby favoring fluid movement from the interstitial space to the capillary lumen. This may minimize the increase in capillary hydrostatic pressure and hence exert a protective effect in the development of interstitial edema.[7] On the other hand, with ARDS there is complete loss of the oncotic gradient and hence loss of this protective mechanism.

Additionally, impaired clearance of interstitial fluid by the pulmonary lymphatics has been speculated, with further accumulation of interstitial edema.[2] The role of surfactant in pathogenesis of ARDS is unknown, but loss of surface active forces and an increase in surface tension may make the hydrostatic pressure of the interstitial space more negative and favor further movement of fluid from the capillary lumen to the interstitial space.[6] All of the above abnormalities are seen in ARDS and help to explain the poor response to therapy in the face of alveolar-capillary membrane damage.

There is an anatomic correlate for the ARDS. The alveolar epithelium, composed of the type I (squamous) and type II (granular) pneumocytes, is separated from the capillary endothelium by an alveolar septum. The septum has a thin portion (the main site of gas exchange) where the basement membranes of the capillary endothelium and alveolar epithelum appear fused, and a thicker section which contains the interstitium components and is the area of fluid flux from the capillary to the interstitial space. Earliest histological changes in ARDS are interstitial and alveolar edema and hemorrhage, with rapid accumulation of high molecular weight proteinaceous substances and cellular debris. There is widespread necrosis of the alveolar epithelium (primarily type I cells) with subsequent hyperplasia and replacement by type II cells. Eventually, hyaline membranes (perhaps induced by such high molecular weight substances as fibrinogen) form in areas of alveolar epithelium damage. Subsequently, there is further thickening of the thick portion of the interalveolar septum, with relative sparing of the thin portion. Lung biopsy at this stage, however, cannot prognosticate permanent damage or complete recovery. In many patients, complete healing ensues, while in others interstitial fibrosis and/or emphysema results. The specific pathologic outcome seems related to nature of injury and pathway of healing.

The pathophysiology of ARDS has been we documented.[1,2,6] The three common features are 1 reduction in functional residual capacity (FRC), 2 impaired gas exchange, and 3) decreased pulmonar compliance (ratio of volume to pressure). Reduced FR relates to several interdependent causes. Initiall interstitial edema accumulates, thereby decreasing th normal pressure gradient from the small airways to th interstitial space. Eventually, patency of airways is n longer maintained; at end-expiration (FRC), thes airways close and remain closed even during th subsequent inspiration due to the large amount c pressure required to reopen them. Distal atelectas occurs with loss of lung volume. At this point, FRC fal below the "closing volume." With additional edema flui alveoli become filled, increasing their surface tensio and making reopening of airways even more difficult. A the compliance decreases, there is a smaller volum achieved for a given transthoracic pressure generated b inspiration.

Hypoxia is the second physiologic feature of ARD Due to interstitial and alveolar edema, many respirato units either do not participate in gas exchang (intrapulmonary shunt) or incompletely participa (ventilation-perfusion mismatch). Thus, blood passe from the pulmonary artery through the capillari without passing fully functioning alveolar units. I addition, there may be a diffusion impairment due t marked thickening of the interalveolar septum.[2] Finall there is a loss of capillary blood volume with increase transit time of blood through the pulmonary circulati and worsening of the ventilation-perfusion imbalanc

Abnormality in lung mechanics (decreased complian and increased elasticity) stems from profou pulmonary congestion and increased alveolar surfa tension. Surfactant is lost and FRC drops below t closing volume. Consequently, large inspirato pressures are needed to reexpand these collapsed unit

Therapy of ARDS demands recognition and (possible) correction of underlying causes and caref monitoring of the patient's respiratory and fluid statu Early treatment decreases morbidity and mortalit Careful fluid management is vital; it should b monitored by Swan-Ganz catheter placement measure pulmonary capillary wedge pressure (P_{AW}) ar to permit determination of mixed venous oxyge tension. Central venous pressure measurement usually too crude an index in this syndrome.

Fluids are adminstered to maintain perfusion of vit organs and to keep the P_{AW} in the normal range (10-1 mm Hg). If adequate peripheral perfusion cannot b maintained with a normal P_{AW}, pressor agents are adde Fluid choice is controversial, but most authors pref crystalloid solutions since colloid can leak into the lu via damaged alveolar-capillary membrane and m increase total lung water content.[2 6 8]

Mechanical ventilation is ultimately required in most all patients with ARDS. High tidal volumes (10-5 ml/kg) seem to prevent and/or reverse atelectasis.[2] he ventilator should be volume-limited; traditionally, ie patient is kept in phase with it through use of orphine sulfate, valium, or a neuromuscular blocking gent, but recently intermittent mandatory ventilation MV) has been successfully employed. Positive end-xpiratory pressure (PEEP) is often required to establish the patency of the collapsed airways. It fords a continuous positive pressure to distend the alls of the airways and alveoli and thus increases the RC. The recruitment of more gas exchange units helps resolve intrapulmonary shunting, improve the ntilation-perfusion imbalance, and thereby raise terial pO$_2$ and decrease the A-aDO (alveolar to terial gradient for oxygen).[1,2,6,8] PEEP may also ssen the pulmonary water content.

Use of PEEP is not without potential hazard. Increased rway pressure, when transmitted to the pleura, may mpress great veins, impede venous return and hence crease cardiac output. This is much more likely in mpliant lungs, since pressure can be readily ansmitted, and in the face of hypovolemia. etermination of best level of PEEP is made by realizing low mixed venous pO$_2$ which implies a decreased rdiac output. If the patient is hypervolemic or rmovolemic, level of PEEP must be decreased. If, wever, the patient is hypovolemic (as suggested by a w P_{AW}), the problem may be corrected with placement volume. The other major complication of EP is pneumothorax or pneumomediastinium, esumably due to overdistension of the relatively rmal alveoli.

Supplemental oxygen is invariably needed; due to the tential of oxygen toxicity, lowest level of oxygen to tain adequate tissue perfusion is used. While arterial O$_2$ is easily measured, determination of mixed venous O$_2$ is an even more reliable index. Low arterial pH may nply metabolic acidosis from anaerobic tissue etabolism and suggest inadequate oxygen delivery to tal organs. Diminished tissue delivery of oxygen can sult from low arterial pO$_2$, decreased cardiac output, creased hemoglobin concentration, and increased finity of hemoglobin for oxygen.[2]

Other modalities of treatment include prevention of electasis with ventilatory support, frequent changing the patients's position, and removal of secretions by dotracheal suction followed by hyperinflation of the ngs to conteract airway collapse.[9] The use of rticosteroids is controversial. Heparin has been ggested to prevent possible microthrombi from udging of blood flow, but its use is hazardous and nfounded, with the possible exception of the velopment of disseminated intravasular coagulation IC). Underlying pulmonary infection must be treated omptly; serial sputum Gram stains and cultures help nical assessment. Finally, extracorporeal membrane yenation (ECMO) has been used in research centers.

In summary, the ARDS is a not uncommon syndrome of diverse etiologies. It may occur in previously healthy individuals. Characteristic is the abrupt onset of respiratory distress, hypoxia, decreasing compliance, and diffuse infiltrates on chest roentgenogram. Successful treatment rests upon early indentification of predisposing clinical setting, prompt and vigorous treatment with meticulous fluid management, ventilatory support, and prevention of complications. The more successful these goals are accomplished, the more likely it is that a favorable outcome will ensue.

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Seminars in Endocrinology and Metabolism

The Continuing Search For the Etiology of Diabetes Mellitus

Stephen E. Dippe, M.D., FACP

Even though diabetes mellitus has been know for thousands of years, the cause has eluded modern science. Through research many of the obstacles are beginning to fall, but definitive answers as to the cause of diabetes mellitus are yet to be discovered.

Diabetes can be divided into two major classifications. Insulin-dependent diabetes, often called juvenile diabetes, can occur at any age, but is more frequently found in the younger age groups. Much more common, however, is non-insulin-dependent diabetes, sometimes called adult onset or maturity onset diabetes mellitus. Even though "non-insulin-dependent diabetes" is the term used to describe this disorder, insulin frequently is needed for treatment. Insulin-dependent diabetes perhaps is better defined as the failure of the beta cell to produce insulin. The non-insulin-dependent diabetic produces insulin and may even have large quantities of insulin but not enough to meet body needs. The non-insulin-dependent diabetic has resistance to the action of insulin.

In studying the inheritance of diabetes, many investigators have found it very frustrating and at times confusing. An autosomal recessive inheritance with variable penetrance has been a concept accepted by many. However, this is speculation. Perhaps the best genetic studies are those that deal with identical twins.[1] Somewhat surprising is that the degree of concordance is greater if the onset of diabetes is after age 40. Only one-half of the twinships 40 years of age and younger are concordant, whereas in the twinships where diabetes developed after age 40, concordance was almost 100%. These studies suggest that non-insulin-dependent (maturity onset) diabetes has a stronger genetic influence than insulin-dependent diabetes. One explanation for the lower concordance rate in the

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From: Family Practice Center, Scottsdale Memorial Hospital,7301 E. 4th St, Scottsdale, AZ 85251

nsulin-dependent diabetic is that environmental factors recipitate diabetes in a genetically predisposed person.

Infectious agents, such as mumps and congenital ubella, have been suggested as a cause for insulin-ependent diabetes. However, the early studies lacked vidence to show cause and effect. Recently, nvestigators have shown a seasonal variation with the nset of insulin-dependent diabetes.[2] From late summer hrough winter more patients are diagnosed diabetics han at other times. These studies lent support to the ypothesis that if the onset of diabetes is indeed easonal, then it may be related to certain infections.

A few years ago, an intriguing study showed a higher revalence of neutralizing antibody titers to coxsackie 4 virus in newly diagnosed insulin-dependent diabetics han controls.[3] Also, there is documented evidence of linical pancreatitis and specific lesions of the islet cells vith disseminated coxsackie B4 virus. However, ollowing a widespread epidemic caused by coxsackie B4 irus in an isolated population, there was no evidence of ny increased prevalence of diabetes mellitus.[4] Thus, the ncidence and frequency of diabetes is not dependent olely on infections and as a result cannot be labeled as a ingle or solitary cause for diabetes mellitus. If viruses ause diabetes in certain individuals, then it is possible ome other factor is needed to sensitize the islet cells to he virus in order to develop diabetes. There is no vidence to suggest that non-insulin-dependent iabetes is in any way related to infection.

Immunologic mechanisms have been put forth over he past few years as playing a role in the development of iabetes. In a recent study, antibodies in the serum to slet cells in patients with insulin-dependent diabetes vere found.[5] At the time of diagnosis, islet cell ntibodies were present in the serum in varying oncentrations in up to 85% of the cases of insulin-ependent diabetes. Also, the detection of these ntibodies diminished over time so that a smaller oncentration (20%) was detectable after three years of he disease. There is an association between persons vith detectable antibodies to islet cells and other utoimmune endocrinopathies such as hypothyroidism, ernicious anemia, and Addison's disease.[6] The ntibodies could represent a response to infected or egenerating tissue and could be an indicator of cell njury only. Also, the antibodies to islet cells and have ot been shown to cause cell destruction. Other ntibodies which seem to be related to diabetes have een described, including islet cell membrane antibodies. ome investigators have described cell mediated eaction.

Finally, in insulin-dependent diabetics, there is an ncreased frequency of certain lymphocyte antigens. A ecent survey indicates that HLA-B8, HLA-B15, HLA-40, and HLA-CW3 are more frequent in diabetics.[7,8] hese findings support the hypothesis that mmunologic events contribute to the development of iabetes.

In the non-insulin-dependent diabetic (maturity onset), such factors as HLA typing and antibody production do not seem to be present. These diabetics have sufficient quantities of insulin and may have very high levels of circulating insulin.[9] There has been no evidence to demonstrate that the insulin is in anyway abnormal or ineffective. What has been shown is that the insulin receptor sites on the cell membrane are impaired. Therefore, this group of diabetics is experiencing insulin resistance with a defect in glucose removal.[10] Obesity plays a significant role in the development of non-insulin-dependent diabetes.

In the insulin-dependent diabetics, the evidence points to a number of possible interrelated etiological factors. It appears that the disease requires both genetic and environmental factors for the development of diabetes. Thus, if the person is genetically primed but does not have the environmental agents to cause the disease, diabetes will not occur. Suggestions have been made that histocompatible antigens on the plasma membrane of the beta cell serve as receptors to viruses or chemicals. It has been postulated that in susceptible individuals certain infections, could precipitate diabetes in an immunologically sensitive individual. Whether or not humeral antibodies cause diabetes or play a role in the development of diabetes has yet to be proven.

In summary, diabetes is made up of two distinct disorders. The most common is non-insulin-dependent diabetes usually found in the older age groups and is related to insulin resistance. Both genetic and environmental factors may be required to precipitate insulin-dependent diabetes which occurs primarily in younger age groups.

Supported in part by the Edyth Bush Charitable Foundation, Inc.

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Thin Needle Cholangiography In The Evaluation of the Jaundiced Patient

Robert A. Sanowski, M.D
Richard A. Kozarek, M.D.
Gene Severino, M.D.
Finis Taylor, M.D.

Editors:
Leon Rigberg, M.D.
Stephen Glouberman, M.D.
George Burdick, M.D.

Evaluation of a patient with suspected obstructive jaundice respresents a challenging clinical problem. Biochemical and histological studies of such a patient frequently fail to differentiate hepatocellular from extrahepatic causes of jaundice. Increasing economic costs and loss of productivity make it essential for the application of techniques which will rapidly define the nature and site of biliary obstruction.

The practicing physician has available, several methods which can define the level and extent of the obstructing lesion. These include transhepatic cholangiography,[1] retrograde cholangiography[2] and mini-laparotomy.[3] Modification of transhepatic cholangiography, using a thin, flexible needle has produced a high diagnostic yield with little patient discomfort and low morbidity.[4] Because of its simplicity, this procedure may be performed with proper training in any hospital equipped with a standard fluoroscopy unit.

Procedure

After premedication with demerol and loca anesthesia with Xylocaine, a flexible, eight-inch, 2 gauge needle with stylet is introduced in the right mid axillary line at the level of the eighth or ninth intercosta space. Under fluoroscopic guidance, the needle i identified and the patient is instructed to stop breathing The needle is then advanced to the lateral edge of th vertebral column at the T_{11}-T_{12} interspace; the patien resumes respiration during the procedure. The stylet i removed and the needle connected to a syring containing 20 cc of Renograffin. The contrast material i injected continuously as the needle is withdrawn until i fills a bile duct. If bile ducts are not visualized, th procedure is repeated a minimum of five times wit alteration of the needle angle. Once the ostruction i outlined, surgery should be done within 24 hours.

Results

Table 1 demonstrates the findings in 36 jaundice patients found to have an obstructed biliary system. A were confirmed at surgery or post mortem Visualization was accomplished in 89 percent. Table represents the findings in ten patients found to have non-obstructed biliary tree. The patients had non surgical causes of jaundice which presented wit obstructive clinical and laboratory features Visualization of the bile ducts was achieved in 50 percen of these. The complication rate was one in 46 or percent. Figure one demonstrates the thin needle in th hepatic duct. Stones are seen in the cystic duct an gallbladder. Figure two is a study of a 68-year-old ma with a retained common duct stone causing obstruciton Figure three is a study of a 70-year-old patient wit

Table 1 - Group A
Obstructed Biliary System

Carcinoma of Pancreas	
Carcinoma of Bile Ducts	
Choledocholithiasis	1
Metastatic Carcinoma	
Biliary Stricture	
Duodenal Ulcer	
Pancreatitis	
Total	3
Successful Visualization	32/36 89%

Table 2 - Group B
Non-obstructed Biliary System

Alcoholic Liver Disease	
Granulomatous Hepatitis	
Hepatitis with Obstructive Features	
Thorazine Induced Jaundice	
Successful visualization	5/10 50%
Complications (Total)	1/46 2.2%

From: Department of Internal Medicine and Gastroenterology, Veterans Administration Hospital, Phoenix, Arizona. Address reprint requests to: Robert A. Sanowski, M.D., Chief of Gastroenterology, Veterans Administration Medical Center, Phoenix, AZ 85012.

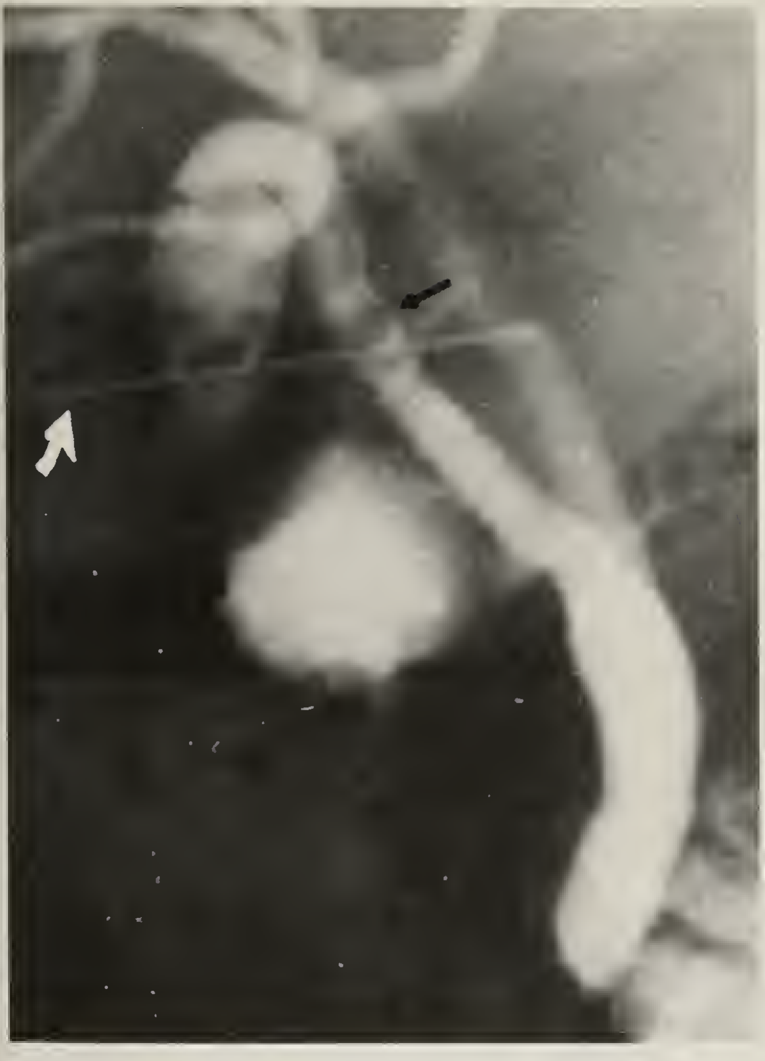

Figure 1

White arrow indicates thin needle in hepatic duct. Black arrow outlines a stone in cystic duct. Stones also seen in gallbladder.

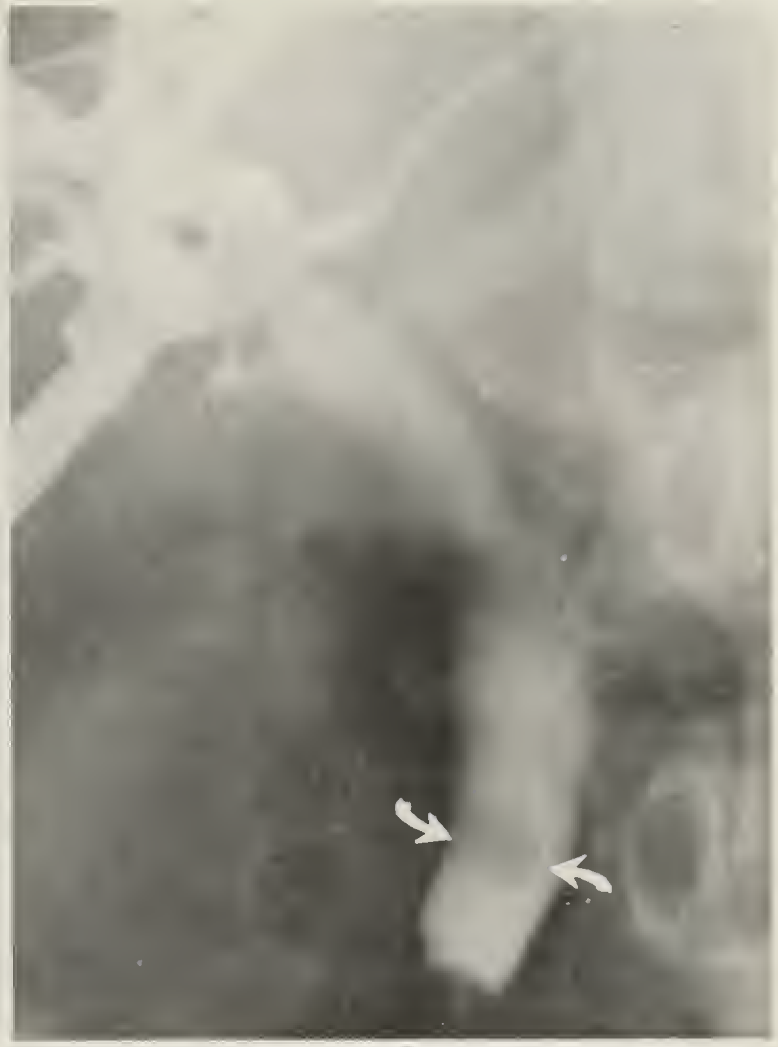

Figure 2

Arrows indicate retained common bile duct stone in a 68-year-old man.

carcinoma of the head of the pancreas. One patient with a non-visualized biliary system developed hypotension and decreased hematocrit two hours after the procedure. She did not respond to transfusions and laparotomy was done. A large subcapsular hematoma was evacuated and bleeding controlled. Study of her liver revealed alcoholic hepatitis with obstructive features. This was the only complicaiton encountered in this series.

Discussion

The differential diagnosis of severe cholestasis is difficult. In cases where the bilirubin exceeds 5 mg%, the oral and intravenous cholangiogram will be unsucessful. A more invasive examination of the biliary tree is required. Ultrasonography and computerized axial tomography have been applied to the differential diagnosis of gallbladder and biliary tract disorders. Results of the non-invasive techniques are promising.[5] False negatives and false positives may be encountered. These techniques may not be available at many community hospitals and patients with obstructed biliary systems should have corrective surgery early in order to avoid degeneration of hepatic function and cholangitis.

The technique of endoscopic retrograde cholangiography is an excellent one for examining both the pancreatic and biliary system.[6] [7] However, it is more difficult to perform, and physicians trained in this examination are not available in many community hospitals. Thin needle cholangiography may be done by a trained examiner in any X-Ray department. The radiologist, gastroenterologist or physician trained in this technique is able to perform the procedure with few complications.

Sucessful visualization of the biliary tree in patients with mechanical obstruciton was achieved in 89% of patients in this series and is comparable to the experience of other groups.[8] Fifty percent visualization in the non-obstructed group indicates there is moderate difficulty in entering the non-dilated ductal system. Failure to visualize the biliary radicals after five attempts should be followed by a liver biopsy, since most of these patients will have nonobstructive causes of jaundice.

This procedure is quite safe, but one complication was encountered early in this group of patients. The frequency of complciation in other series ranges from zero to 8% and includes fever, hemorrhage, bile peritonitis, bile leakage and cough.[8] Most are treated conservatively. Surgery on dilated ductal systems is made easier by localizing and defining the site of obstruction.

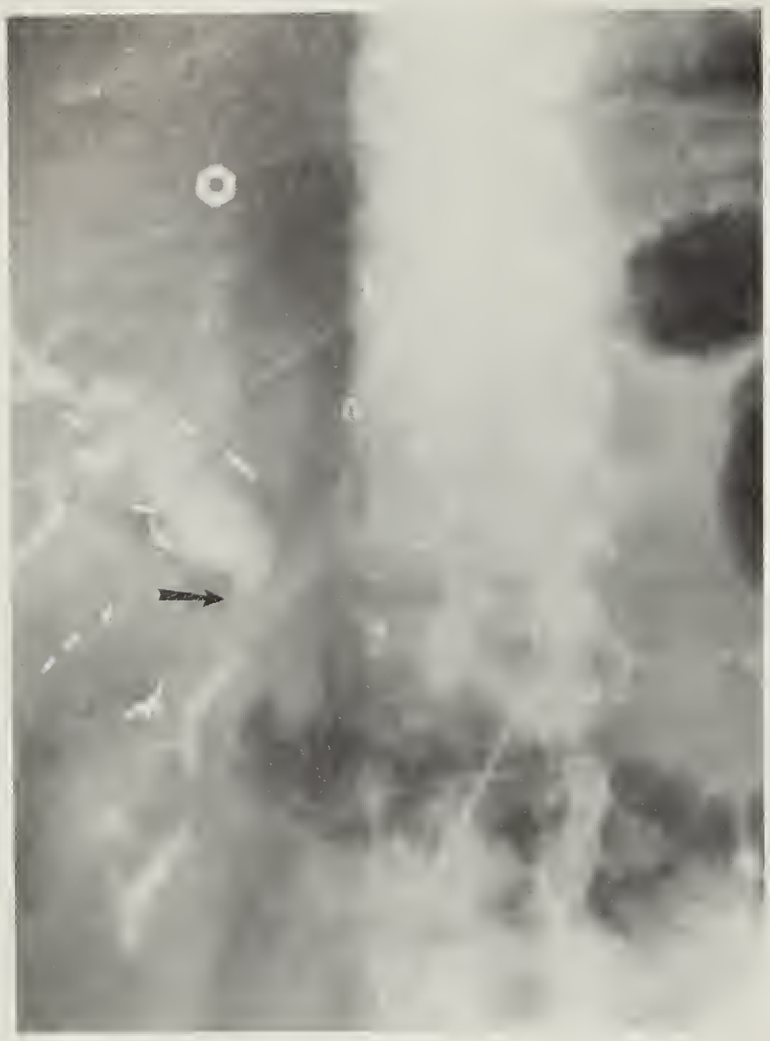

Figure 3

Arrow indicates obstructed common bile duct in a 70-year-old patient with cancer of the head of the pancreas.

Summary

Thin needle cholangiography is indicated for diagnosis of suspected extrahepatic biliary obstruction in practically all patients if there is question as to the diagnosis. Failure to enter the ducts on several attempts strongly suggests absence of bile duct dilation. It is an extremely valuable procedure which provides diagnostic information easily and safely. Thin needle cholangiography can differentiate medical versus surgical cholestasis eliminating the need for surgical exploration. It provides a simple, direct visualization of the biliary tree and may be performed in the radiology department of any community hospital by physicians properly trained in the technique.

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AM *Neurology*

Intracranial Aneurysms: Diagnosis and Treatment

William B. Helme, M.D.

Editors:
Betty F. Ball, M.D.
Barry Hendlin, M.D.
Lawrence Z. Stern, M.D.

The following article is based on a consecutive series, extending over a period of seven years, of surgically treated intracranial aneurysms with no mortality. This study was published in the June 1978 issue of *Neurosurgery* (No. 1). It concerns a subject of special

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From: Neurological Surgeons, P.C., 345 E. Virginia Ave., Phoenix, AZ 85004

nterest to neurosurgeons, but one of which general physicians should be aware as they have first contact with these patients.

Almost always the presence of an intracranial aneurysm is announced by subarachnoid hemorrhage. This is a calamitous event manifested by a sudden and severe headache. A recent patient described it as, "My head exploded." Symptoms of a nonruptured aneurysm nclude visual loss, ophthalmoplegia and anisocoria. Following a bleed, the patient's condition may vary from alertness to deep coma, depending largely on the volume and location of the hemorrhage. Usually there is no focal neurological deficit unless the bleed has been nto the substance of the brain rather than into the subarachnoid space. A spinal tap will produce gross blood and confirm the diagnosis. A computerized axiotomography scan will usually demonstrate blood in the subarachnoid pathways, possibly the aneurysm tself, and eliminate the need for lubar puncture which may involve some risk in the presence of increased ntracranial pressure. Usually four-vessel cerebral angiography performed within a few days of admission o the neurosurgical unit will demonstrate the source of he hemorrhage. Bed rest, sedation, control of systolic hypertension greater than 140 mm. mercury and avoidance of stress are ancillary measures employed nitially in the treatment of this condition. Aminocaproic cid is usually used to inhibit clot lysis and reduce the ikelihood of recurrent hemmorrhage.

The great majority of neurologists and neurosurgeons agree that the best way to prevent ebleeding is to clip the aneurysm. This can be a ormidable surgical procedure and requires careful planning and technique. In most neurosurgical centers, ecent operative mortality in large series has been about 5%.[2] There has been a substantial improvement in outcome since the advent of the operating microscope but the primary factors are the level of consciousness of he patient preoperatively and the location and onfiguration of the aneurysm. Postoperative omplications most frequently arise from cerebral schemia resulting from arterial spasm or compromise of he parent or perforating arteries by the aneurysm clip.

In summary, subarachnoid hemorrhage is not rare nd may occur in any age group. Invariably it will be nnounced by the sudden onset of "the worst headache 've ever had." Failure to recognize the ominous nature of such a headache can lead to inadequate treatment and isaster from recurrent hemorrhage. The results of nicrosurgical treatment of intracranial aneurysms have mproved to the point that overall operative mortality in arge referral centers approximates 5%.

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Obstetrics and Gynecology

Problems of the Vulva

Edward A. Friedrich, Jr., M.D.

Donald J. Ziehm, M.D., Editor

Tradition has it that there is really nothing new in medicine, but that we constantly rediscover the old and forgotton. Many physicians seem to persist in that belief when dealing with vulvo-vaginal disease. But possibly we are relearning what physicians years ago knew, things we have somehow forgotten amidst the plethora of scientific advances of the recent past. Many gynecologists approach vulvo-vaginal disease with a one-eyed look at the problem -one treatment for vaginal disease, one for vulvar problems. If the standard therapy isn't effective, something esoteric must be happening and therefore nothing will work. This approach is being replaced by the diagnostician who carefully evaluates the problem and then applies the proper therapy. This paper will review some of the older, and perhaps some new, methods of dealing with vulvar disease.

From: The Medical College of Wisconsin, Dept. of OB/GYN, Dr. Friedrich, Associate Professor. Presented at *New advances in Obstetrics and Gynecology*, Phoenix, AZ, February 14, 1979.

Condyloma An old disease, described in all of the standard textbooks of gynecology. Therapy is relatively unchanged; Podophyllin has been used for many years. Podophyllin is a mitotic poison, highly effective when applied to growing lesions that are actively undergoing mitosis. Older condyloma (the flat, pigmented, smooth lesions) will not respond nearly as well. The cells are not reproducing rapidly enough. However, Podophyllin is not without its toxicity. When applied to condyloma in excessive amounts, neurotoxicity is a potential hazard. Use in pregnancy may lead to fetal damage or death. Numerous reports in the literature attest to both these problems. So caution is avised.

Management of condyloma: 1) The proper use of *Podophyllin*. Applied in small amounts on young, external lesions, rapid regression can be anticipated. Excessive amounts might be dangerous. 2) *Laser* (an instrument in search of an application?) certainly works on condyloma. They can be destroyed just as easily as with any other treatment. However, is its use cost-effective when compared to the old fulguration unit? Furthermore, treatment with the Laser does necessitate use of local anesthesia. 3) *Electrical Fulguration* is cheap, simple, and highly effective, with a low recurrance rate. The lesions are hyfercated and then scraped off with a #15 scalpel blade. 4) *5 Fluorouracil (Efudex)*. Like Podophyllin, it is a mitotic poison. Thus its use should be restricted to young, actively growing lesions. 5 FU is probably safer than Podophyllin since neurotoxicity is avoided. Application once daily for two weeks may produce significant regression in both number and size of the growths. Regression may occur to the point that complete eradication may be achieved with fulguration. So, as an adjunctive therapy, 5 FU may be utilized with some success. 5) For the very large lesions there is no substitute for hospitalization, general anesthesia, and fulguration with a large Bovie unit. If this approach is necessary, the use of a Bovie with a long loop is suggested so that damage to deeper tissues will not occur. The condyloma can be easily and rapidly looped off, where this might take hours if attempted as an office procedure.

Herpes. A continuing problem with no effective therapy. It is viral in etiology, sexually transmitted, easily identified, and potentially harmful to neonates. The same ulcerations that appear on the skin of the vulva can also be present in the urethra and bladder. For this reason mny patients have severe, excruciating dysuria, occasionally leading to urinary retention. If catheterization is necessary, the use of a supra-pubic catheter is suggested; it does not traumatize the ulcers already present within the urinary tract like an indwelling catheter might do.

Management of Herpes: 1) *Analgesics*. 2) *Burrough's Solution* is very soothing whenever an open sore lesion is present. The wet compresses of Burrough's solution will dessicate the ulcers and seal off the raw nerve endings. Considerable comfort can be obtained. 3) *Steroids*. They are anti-inflammatory and may promote healing. 4) No specific therapy is available, although many remedies have been proposed. 5) *Ether*. A recent study reported no demonstrable effect on the course of the disease. Furthermore, the treatment is quite painful. 6) *Thymol 4% with Chloroform* has been used in an attempt to destroy the lipid envelope of the virus. Some clinicians feel that Thymol alone works as well. A recent paper suggested that straight Thymol (Listerine) applied full strength to the lesions was helpful. 7) *Cryocautery* is not useful. 8) The *Laser* has been tried unsuccessfully. The Herpes ulcers may recur at the site of the Laser application, and the Laser ulcer may be very painful. 9) *Immune stimulators* - vaccination with smallpox or BCG. Unfortunately, neither alters the course of the disease nor affects the rate of recurrence. 10) *Dye-light Therapy*. In a recent double blind study performed in Houston no difference was noted between the use of photoactive dye and a placebo. The question of carcinogenicity also remains to be settled satisfactorily. Histologically, biopsies have shown that Herpes may indeed produce epithelial atypia, but the specific treatment probably has no effect on the cell changes. The dye probably is not a carcinogen, but it is also reatively ineffective therapy. 11) *Betadine* will inactivate surface virus, and may prevent surface spread of the lesions. The incidence of superimposed bacterial infection may also be decreased. And it gives the patient something to do while the disease gets better. The lesions are swabbed twice daily with Betadine swabsticks. If the ulcerations are in the vagina or on the cervix, Betadine douche is given twice daily. 12) *Wine* Recent work by a Canadian group showed a lethal effect on the Herpes virus following applicaiton of red wine. White wine was even more effective, while grape juice was the most effective. Could it be the formaldehyde present in these liquids that caused these results? In difficult cases this might be worth trying.

Molluscum Contagiosum. A virus caused lesion that is sexually transmitted. Transmission occurs not so much from actual penetration in intercourse as in close skin contact. While easily diagnosed by the characteristic central punctum or umbilication filled with a semi-solid white material, they may occasionally be large and without the central dimple. The diagnosis is then much more difficult. These lesions are rather subtle and are usually asymptomatic. Autoinnoculation commonly occurs with rubbing or scratching. If untreated, spontaneous regression usually takes place. Histologically, the lesion enlarges by compression of the underlying dermis, forming a pseudocapsul. The "whitehead" can be removed from its capsule by inserting a large bore needle at the periphery of the lesion and lifting upward. This can be performed with little discomfort, without anesthesia. Following extraction each area is cauterized with a AgNO stick.

Cutaneous Candida: This is found frequently in diabetics. Therefore, a Glucose Tolerance Test should routinely be performed in any patient with overt and evere cutaneous candida.

artholin Duct Obstruction: Marsupialization, an old ried and true method of treatment, is associated with a ecreased rate of recurrence. An accessory duct is onstructed which drains the obstructed portion of the land. It is important to remember that the incision is *not* ade on the skin of the libia majora. Since the normal uct drains into the vestibule adjacent to the hymen, the arsupialization should be performed in that area. nother method of office management is the use of the Vord catheter (the end of the pediatric Foley catheter). he vaginal mucosa in the vestibule is infiltrated with cal anesthesia. A small stab wound is made into the yst cavity, the cyst flushed out, and the Word catheter serted. the balloon is inflated just enough to keep it in lace. Distention of the cyst cavity with the balloon hould be avoided as this may cause a great deal of iscomfort. The end of the catheter is then tucked into he vagina and removed in six weeks. Essentially a arsupializaiton has been performed, but in a much horter operative time. A small accessory duct remains the same anatomic location in which the normal duct vould empty. The Word catheter is available, dividually sterilized, by American Cystoscope Makers, nc.

Oncology

Adenocarcinoma of the Stomach
Current Knowledge and Recent Advances

Frederick R. Ahmann, M.D.

Editor:
David Alberts, M.D.

Gastric carcinoma is a world-wide health problem. For example, in Japanese males, 56% of all cancers arise in the stomach. In the United States, 15,000 people were estimated to have died from gastric carcinoma in 1977 (seventh in cancer-related deaths), with an incidence of six cases per 100,000.[1] The purpose of this paper is to review the current knowledge and recent advances in *adenocarcinomas* of the stomach (which comprise over 95% of all gastric malignancies).

It is not known conclusively why there is such a marked geographic variance in incidence of gastric adenocarcinoma. However, a person's risk is markedly increased by spending the first 10 years of life in an area

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From: Sect. of Hematology & Oncology, Dept. of Internal Medicine, Univ. of Arizona Health Sciences Center, 1501 N. Campbell Ave., Tucson, AZ 85724.

where, apparently through methods of treatment or preparation of food, substances (nitroso compounds?) are presented to the stomach, causing precursor lesions which over 30-50 years evolve into a malignant neoplasm.[2]

There are four gross patterns of appearance of stomach carcinomas: ulcerative, polypoid, scirrhous, and superficial. The Japanese have long recognized the latter, superficial carcinoma, as a special entity with a high probability of surgical cure even in the face of spread to regional nodes. Only recently have western countries documented this entity in 10% of cases.[3]

For the past decade, it has been hoped that tumor-associated antigens would provide a reliable screening test for gastric carcinoma in high-risk patients (patients over the age of 60 with gastrointestinal complaints, especially men, and patients with pernicious anemia). However, analysis of the Framingham population who subsequently developed stomach cancers, indicated that carcinoembryonic antigen, alpha fetoprotein, and human chorionic gonadotropin assays not only lacked specificity but gave lead times to diagnosis of only months, not years as would be necessary to significantly improve prognosis.[4] Symptoms of gastric carcinoma remain frustratingly vague and nonspecific until signs of obstruction appear, usually indicating an advanced state.

A problem that is often faced is how to approach the patient with the diagnosis of gastric adenocarcinoma made on the basis of cytology or biopsy. No definitive criteria have been proposed to provide an easy answer to this question, but several facts are known which allow individual cases to be evaluated more effectively. A reasonable approach is that if good screening for distant metastases is negative, then surgery is clearly indicated, not only for potential cure but, even if only palliative, to increase the chance for 1-year survival. A complete evaluation might reveal no suspicious left supraclavicular or left anterior axillary nodes, no skin lesions around the umbilicus, a negative chest x-ray, a negative bone scan, a negative brain scan (if symptoms or signs warrant one), and a negative liver scan (which is correct 95% of the time in gastric carcinoma in predicting liver involvement).[5] Surgery candidates must be selected carefully because of operative mortality rates of up to 30% and morbidity rates approaching 70%.

Surgery does offer the only chance for cure in this disease. Unfortunately, operative statistics have not changed significantly in 20 years, with 80% of patients usually undergoing some surgical procedure with resections attempted in 50%. Only 20%, after surgery, are thought to have been potentially cured but recurrence data indicate that cure is obtained in only 25% of that number. Five-year survival for all patients is 7%, with median survival of only 3 months. Subtotal and radical subtotal gastrectomy have given the best survival rates with the lowest mortality. The more distal the lesion in the stomach, the better the chance for survival.[6]

Radiation therapy as adjuvant to surgery or as singl modality treatment does not increase survival in gastri carcinoma but does play a role in the relief of pain, th relief of obstruction, and the control of bleeding. In a adjuvant study at the Mayo Clinic, radiation therap plus 5-FU did increase survival by 6 months as compare to 5-FU alone, and further evaluations of combinatio modalities including radiation therapy are bein performed.[7]

Results with chemotherapy, in either an adjuvant o primary modality role, are slightly more encouraging. I recurrent or advanced gastric adenocarcinoma, 5-FU mitomycin C, BCNU, CCNU, and adriamycin as singl agents have all had response rates of 18% - 30%, with response durations lasting less than 4 or 5 months. Som 30 other drugs have been evaluated as single agents and show minimal activity.[8] More promising are *combination* of the active agents. Thus far, the combination of 5-FU adriamycin, and mitomycin C (FAM) has demonstrated the highest activity. The response rate has been reported as slightly better than 50%, with surviva increased from 6 months in control patients to over 1 months.[9] Adjunctive chemotherapy after surgery with combinations of drugs is still being evaluated, but hold promise of increasing survival duration.

Summary

Gastric adenocarcinoma, while decreasing in incidence in this country, is perhaps the world-wide leading cause of cancer-related death in men. Whereas diagnostically, gastric cancer often must be distinguished from gastric ulcer, more frequently gastric cancer has few signs or symptoms until fa advanced. Surgical therapy offers the only chance fo cure; however, at surgery only 20% are potentially cured and, of those, only 25% are actually cured. Radiation therapy may play an as yet undefined role in combined modality therapy with the main therapy for advanced or recurrent disease being combination chemotherapy Although no one drug regimen stands above the rest with aggressive therapy, responses can be seen in approximately 40% - 50% of patients and surviva prolonged in terms of months. Surgical adjunctive combination chemotherapy may be shown to be beneficial in ongoing studies.

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Psychiatric Disorders

The Sabotage of Scientific Method

William B. McGrath, M.D.

Most people presume that our objection to socialized nedicine is jealous and self-seeking. Naturally we resist he pushing of regulatory agencies to take control of our rofession and our work.

Our real protest, however, is based on a much deeper ut seldom articulated concern: *Socialized medicine ceases to e medicine and becomes sociology.* This is already happening nd it is dreadful to contemplate.

The medical model is the epitome of scientific method. Discoveries which have been of immense value to nankind have almost invariably followed this model, his method. Hippocrates, Celsus, Galen, Edison, the Wright brothers, — these men were tinkerers. They spent their time not in libraries but in the laboratory or clinic. Their theories came as a result of infinitely patient observation of processes accessible to the human senses, things which in nature are individual, ultimately unique. The facts of life are mute, nonverbal.

By contrast little that contributes to human welfare has been accomplished by philosophy or sociology, by the manipulators of words and numbers.

The vast philosophical systems are, in a way, like infants. To the philosopher, as to the infant, the universe is peopled by powerful unseen forces that, for good or ill, control our destinies. From great generalizations the philosopher may string long necklaces of syllogisms and deductions. His logic may be impeccable but without reference to reality and lacking any useful substance. One cannot bring to mind any philosophical system or ideology which has lessened the fearsomeness of this world or responded to the cry for more liberty, equality, fraternity.

Scholarly and altruistic phiolosophies become distilled into fervent slogans, and more harm than good is in store.

If philosophy has elements of infantilism, sociology seems somewhat adolescent. The social "scientist" and the adolescent share the same core problem, the struggle for and against individuation.

Sociology cannot find the individual, yet only the individual is accessible to our senses and hence scientifically real. The truths of sociology are only truths by definition and rarely by demonstration or replication. One reads of "statistical proof" of something. Nonsense; statistics can show only averages or trends or probabilities.

A well fed and cynical demagogue proclaims that everyone has the right to the best of medical care, and the gullible gulp down the bait. Grandiloquent statements like that are ill defined and meaningless. Rationalizations for them, based on similarly undefined terms in the constitution (life, liberty and the pursuit of happiness) would apply with equal force to everyone's "right" to the best of all goods and services. We'd have class action suits to halt discrimination against the "the poor" in hotels, in fancy resstaurants, in clothing stores, markets. First we'd ask for "legicare" and "funicare."

Sociologists are not grounded in science. The typical proposition, "poverty breeds crime," is no more true or significant that the opposite, "crime breeds poverty." (Beacuse he does not work the ordinary criminal remains in destitution or drifts toward it).

The social "scientist" works in the never-never land of arbitrary groupings: the disadvantaged, the ethnic or minority groups, the criminal, the mentally ill, the diabetic. Such groupings exist only in his imagination. A person with any dignity would resist being dunked in any such pool at the cost of his identity. Has any individual really benefitted from being classified? Most social groupings, protesting the opposite, just perpetuate the antagonistic divisiveness of (popular

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From: Camelback Hospital, 5051 N. 34th Street, Pheonix, AZ 85014.
Dr. McGrath, Medical Director.

This article is one-sided. On the pyramid of human caring the relevant and worth while contributions of Philosophy and Sociology will be considered at another time. WBM term) polarization. Sociology has yet to achieve any discernible influence on the prevalence of war and crime and cruelty and unfairness in the world.

Yet there are powerful forces dragging the professions back from science into sociology. Because they are mostly well-intentioned they are the more sinister. It is not safe in this troubled world to be guided by lofty sentiments instead of clear reasoning.

Medicine is already infested by sociology. Our hospital and staff doctors have to meet criteria spelled out in gaseous verbiage by the Joint Commission on Accreditation, the Medicare survey teams, the office of Continuing Medical Education, the health and safety codes at all governmental levels, the various agencies, insurors and the specialty societies.

A doctor might assume the awful responsibility of treating a life threatening or potentially crippling disease. (Correction: One treats the person, not the disease.) The clinical outcome might be gratifying.

Now some constipated clerk, who has no medical training in general and no firsthand contact with the case, may decide that the hospitalization and the patient's treatment were unnecessary or inappropriate.

The decision is far removed from the reality of the case (a process, by the way). What can put you out of business is not your medical competence but your choice of words in filling in the medical record. Whatever explanations or appeals ensue, the clinical problem will never be reviewed, only the frozen language of its documentation.

Of the fabled fifty minute hour we can now spend only ten minutes in contact with the patient and fifty minutes writing unrealistic promises and padded nonsense to satisfy the utilization reviewers. They judge not what we do but only what we say, and this is not intelligent.

The statistician's general statements about various labels (diseases, therapies) are often nonsense when applied to the individual case — and there is no other.

Problem oriented medical record keeping forgets the flesh and blood person while it lends itself to computer recording for the convenience of statisticians and intermediate agencies. Community psychiatry is not psychiatry; it is sociology. Therapies which overlook the individual, such as those of interpersonal relationships and groups, are treating scientific fictions and getting mostly fictional results.

No;, if a man is ill, please do not give him compassion instead of penicillin and do not bind his wounds with directives from HEW. A sick person needs the dispassionate knowledge and skill of a doctor trained in science. He will still see the patient as a unique individual who, as such, might teach us something new and important.

If medicine gets dragged any closer to the quagmire of sociology they'll find us on the rooftops of our institutions, cutting out paper dolls and sailing paper airplanes at the (odious term) regulatory agencies.

Special Articles

A Personal View of Medicine in the U.S. Past Present and Future

Merlin K. DuVal, M.D.

American medicine consists of tw principal components: a private sect that is self-determining and whic operates as a franchised monopoly; and public sector which exists to meet tho needs that either cannot or will not be m by the private sector.

As is true in most developing nation whatever was known about medicine w the exclusive property of those wh practiced it at the time of its birth. Mo medical knowledge was passed from or generation to the next by dire instruction of one student by or physician. The circulation of medic knowledge by means of the printed ar spoken word was greatly limited; ar institutions of higher education, with few notable exceptions, did not constitu a part of the mainstream of medic knowledge. In 1847, individual practici physicians joined together for th purpose of increasing their capactiy communicate with one another, advan medical knowledge, bring standards int the practice of medicine, and otherwi take such steps as were necessary upgrade and strengthen their professio Today, 131 years later, the Americ Medical Association still pursues tho objectives and continues to serve as th most prominent voice representing th private sector of American medicin Because of its relatively early arrival the American scene, this associati enjoyed the unique opportunity fostering the further development American medicine as an essential private and self-determining professi unchallenged in its supremacy in medic matters.

From: University of Arizona, Tucson, 85724. Dr. DuVal, Vice President for Hea Sciences. This article is an abridgement of manuscript presented at the XXVI Ann Convention of the Medical Society of United States and Mexico in Guadalaja Jalisco, Mexico, November 16, 1978.

Such freedom has, of course, permitted e development of a very strong rofession. It has also made possible a reat deal of experimentation and variety the manner in which the private sector istributes health services. Physicians ay work as individuals, solo ractitioners, or in small groups that take e form either of single discipline ractices or multidiscipline group ractices. Recently, some physicians have mbined into larger organizations for e purpose of creating closed panels to nder comprehensive services to large roups of citizens who choose to enroll as embers. In many such instances the aditional fee for service mode of ayment has been displaced by repayment schemes.

In summary then, American private edicine is characterized by the high egree of freedom, autonomy and rofessional self-determination that are joyed by each of its practitioners and stitutions, relatively free (at least until ry recently) of external regulation and ntrol.

In the public sector of medicine in the nited States, there are three levels of vernmental medicine, each of which nds to subserve a somewhat different nction. At the most local level is the unty, or in a few specific instances city, vernment. For the most part, local vernment assumes responsibility for oviding both ambulatory and general edical and surgical hospital care for the or, and it operates community-wide ograms of preventive medicine and blic health, including sanitation and vironmental control.

The next level is state government. ntil recently, when public financing of edical care began to assume increased ominence in the United States, the led of state government was primarily ditive, or complementary, to the rvices provided by county government d found expression in the tablishment of institutions and facilities r the care of individuals with chronic sabling diseases such as tuberculosis d mental illness. State government also rticipates in public health and eventive medicine programs; operates boratories; and is involved in sanitation d environmental control programs.

For approximately 150 years the deral government has also been making contribution to the American health dustry but, until quite recently, its role as rather specific and directed at eeting the requirements of designated eral beneficiaries. In 1798, the Federal vernment created the United States blic Health Service and charged it with sponsibility for providing medical rvices to sick and disabled seamen, and otecting the nation's boarders against e importation of diseases the were reign to American soil. Over the cceeding years, the Federal government adually undertook a somewhat broader blic health responsibility by tablishing closer relationships with ate and local health departments for the rpose of controlling communicable diseases and improving sanitation. Next, it adopted programs to meet what it construed to be its obligations to provide medical services to specific beneficiaries such as the native-born American Indian, members of the armed forces and the veterans of America's wars. Programs for the care of these federal beneficiaries are still very prominent in Federal medicine today.

The establishment of the National Cancer Institute in 1937 opened a new era for the federal role in health because it offered direct federal support for biomedical research. This move culminated in the creation of the extramural programs of the National Institutes of Health, which programs supported research in the private sector. Almost simultaneously, the Federal government began moving more heavily into the field of regulation, food and drug inspections and control of the environment through programs designed to combat pollution of air and water. Even more recently, political and social pressures in the United States resulted in the development of federal programs designed to meet the health problems of particular population groups such as migrant farm workers, mothers and children among the poor, crippled children, those afflicted with alcoholism and drug abuse and the mentally ill.

Since the role of the U.S. government in health has become so complex in recent years, it might be helpful to clarify my description of this role by noting that the U.S. government now does five things. First, it has accepted an important responsibility for providing health services *directly* to certain specific beneficiaries. The government employs many thousands of physicians, dentists and other health personnel and operates hundreds of health care institutions for these purposes. The Department of Defense has a medical establishment that is now scattered throughout the world. The Veteran's Administration operates one of the world's largest closed-systems for the direct provision of health services to veterans. The U.S. Public Health Service dispenses care directly to merchant seamen, federal prisoners, members of the Coast Guard, and American Indians. Even at this time, the Public Health Service is experimenting with a National Health Service Corps which assigns physicians to render medical services to persons who live in geographically underserved areas.

Second, the Federal government provides health care *indirectly* through grants and contracts to private organizations and to state and local health departments. These units then provide health care to specific population groups such as migrant farm workers, the inner city poor, mothers and infants, crippled children, and others. Both the Veteran's Administration and the Department of Defense also have the capability for purchasing specific services from the local private sector so that they will not have to duplicate, unnecessarily, such services within their own system.

Third, the Federal government has undertaken a major role in the development of health resources. The National Institutes of Health oversee the largest enterprise in the world in support of both basic and targeted biomedical research. The Health Resources Administration supports the production of traditional and new forms of health manpwer and supports the construction of community hospitals through the federal Hill-Burton program.

Fourth, The Federal government has taken on a progressively increasing responsibility for quality control through the inspection and regulation of those instruments, devices and consumable supplies that constitute a part of the paraphernalia of the health industry and which are not otherwise controlled by the private sector. The Department of Agriculture now inspects and grades all meat and poultry products. The Food and Drug Administration reviews, inspects and regulates the flow of drugs; inspects the processing of foods and regulates the production of cosmetics. It also has responsibility for the regulation of hazardous substances and for radiological safety. The federal government also monitors the purity of water and air.

Fifth, during the last two decades there has been a growing feeling in the United States that reasonable and convenient access to quality health services should be among the rights of the American people. Public conern has now reached a point such that a national debate is underway as to how best to achieve such an objective as a matter of public policy. Because we have a medical profession that is intrinsically self-determining, and is thus in conflict with a public policy that would mandate coequal access to its services, the Federal government finds itself in the position of attempting to reconcile these competing objectives. Simply put, the government has two choices: using its extrordinary influence and resources to achieve reform of the traditional institutions for distributing health services, or else taking over control of the health industry. Perhaps because of its heritage we have chosen, thus far, to pursue the first of these alternate options. As a result, we have recently seen a plethora of new federal programs designed to encourage, indeed stimulate, modifications and reforms of the traditional American institutions as, for example, the Regional Medical Programs for cancer, heart, stroke and kidney disease; comprehensive health planning; professional standards review organizations; emergency medical services program; the development of health maintenance organizations; and the introduciton of new methods for financing medical care, most notabley the American Medicare and Medicaid systems.

Space does not permit a proper evaluation of the impact such programs are having on the American scene; although many of us feel that the degree to which these programs are successful will, in all likelihood, determine whether the Federal government will go on to adopt a national health insurance program for the purpose of paying for medical care, or a National Health Service program for changing America's health delivery system.

The contemporary American dilemma can, therefore, thus be summaried as follows: American medicine is credited with having made a strong contribution to the expansion of the scientific and technological basis of medical. practice. Unfortunately, these advances had the paradoxical effect of whetting the American appetite for universal access to everything that medicine could make available at precisely the time that the dynamics of American medical education and practice were moving in the opposite direction. One might say, then, that the stage is currently set for a major contest in the United States; a contest betwe the traditional right of the medic profession to remain free and sel determining, and the contervailing rig of the people to reasonable access to th services of that profession through geographic and specialty redistribution its physicians. How this contest will b resolved remains uncertain.

State of the Art

Enzyme Inhibitor Therapy Of Hypertension

Eric H. Prosnitz, M.D.

The pathogenesis of essential hypertension remains an enigma. Multiple variables effect blood pressure and it is likely that essential hypertension as we currently perceive it encompasses a heterogeneous group of disorders. Two of the many regulators of blood pressure are bradykinin, a vasodepressor, and angiotensin II, a vasopressor.

Kallikreins, of various origin, act on circulating kininogens to produce circulating bradykinin which is then degraded to inactive metabolites by two peptidases, kininase I and kininase II. While the role of the kallikrein -bradykinin system in hypertension is as yet unclear, the renin angiotensin system has a definite role in the pathogenesis of some hypertensive conditions, e.g. renovascular disease, renin secreting tumors, and the hypertension occurring with the use of oral contraceptives.

The Renin Angiotensin System

Renin is a proteolytic enzyme that is synthesized stored, and secreted by the juxtaglomerular apparatus o the kidneys. Renin cleaves four amino acids from ar alpha 2 globulin secreted by the liver thereby producing angiotensin I. Two additional amino acids are ther removed from the angiotensin I molecule; producing angiotensin II. This reaction occurs primarily in the lung, where pulmonary vascular endothelial cells contain high concentrations of converting enzyme Angiotensin II then binds to arterial receptors causing vascular smooth muscle contraction, an increase ir peripheral vascular resistance, and a rise in blood pressure. Interestingly, the structure of converting enzyme has been shown to be identical to kininase II.[1]

Laragh has proposed an indirect measure of the role of angiotensin in hypertensive patients.[2] This renin profile compares levels of peripheral vein plasma renin activity

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From: Hypertension Clinic, University of Arizona, Health Sciences Center, Depart. of Internal Medicine. Dr. Prosnitz Asst. Professor of Medicine.

with 24 hour urinary sodium excretion. Intravascular olume status alters renal renin secretion and renal ubular sodium reabsorption such that peripheral vein enin levels, an imperfect reflection of renal renin ecretion, are inversely correlated with renal sodium xcretion. A number of investigators have shown pproximately thirty per cent of essential hypertensives o have lower than normal peripheral renin levels and an dditional fifteen per cent to have higher than normal evels. It should be kept in mind that the limits of normality vary with characteristics of the population tudied (for instance, age and race). Furthermore, normal renin patients generally respond as well as high enin patients to drugs which decrease renin synthesis. These similar responses may reflect extra renal sites of action of these drugs. Thus, the diagnostic and herapeutic significance of the renin profile in patients with essential hypertension is usually minimal. Renin profiles are not a necessary step in the routine diagnostic evaluation of these patients.

Saralasin - An Angiotensin Antagonist

An alternative to reducing renin secretion in treating essential hypertension is preventing the end organ vasoconstrictor response to angiotensin II. This can be accomplished with competitive inhibitors of angiotensin I, of which the best studied is saralasin. Saralasin is an analogue of angiotensin II with two amino acid substitutions in the octapeptide sequence. Clinical utility of saralasin is limited. Although angiotensin mediated hypertension generally is manifested as a hypotensive response to administration of saralasin, there is considerable overlap in response between ndividuals. In addition, volume status of the patient should be known for optimal interpretation of results. A patient with excess intravascular volume, for instance, may have a pressor response to saralasin due to large numbers of unoccupied vascular receptors for angiotensin II, and the partial agonist activity of saralasin. Saralasin must be given parenterally and therefore is not suitable for chronic therapy.

Development of the Enzyme Inhibitors

Concurrent with the recognition of the limitations of saralasin, interest has been increasing in a class of compounds which inhibit the enzymatic conversion of angiotensin I to angiotensin II. Encouraging results with these drugs has led some to again champion the role of the renin angiotensin system in the pathogenesis of essential hypertension. However, a review of the development of the enzyme inhibitors is instructive in this regard.

In the mid 1960's Ferreira, an investigator in the department of pharmacology of a South American medical school, was studying the actions of bradykinin. As part of those experiments, venom (containing slow reacting substance) from a pit viper, Bothrops jararaca, was employed. A serendipitous finding was that the venom itslef enhanced (in vitro and in vivo) the action of the bradykinin. In one set of experiments synthetic bradykinin was given intravenously to five cats; resulting in a mean blood pressure reduction of 20 mmHg. The same dose of bradykinin, infused after pretreatment with snake venom resulted in a mean blood pressure reduction of 72 mmHg. This discovery of an undefined hypotensive substance was published in 1965 in a article entitled *A bradykinin-potentiating factor (BPF) present in the venom of Bothrops jararaca.*[3]

Three years later it was found, using in vitro bioassay techniques, that bradykinin potentiating factor (BPF) also inhibited the conversion of angiotensin I to angiotensin II.[4] In 1970 Ferreira and colleagues successfully isolated from the snake venom nine biologically active peptides which had differing potency with regard to enzyme inhibition.[5] The authors stated, "Since limited proteolysis reactions occupy a central role in the release and inactivation of the circulating hormones bradykinin and angiotensin, inhibitors of these reactions may be used to demonstrate the participation of these hormones in various physiological phenomena. Such enzyme inhibitors may also prove to be therapeutically useful in pathological conditions such as inflammation and hypertension."

Thus, while the potential antihypertensive properties of these polypeptide enzyme inhibitors were recognized; it is clear that these properties were not confined to the renin-angiotensin system.

Teprotide

Shortly thereafter a synthetic enzyme inhibitor, Teprotide (SQ20881), was developed and studied with regard to its effects on angiotension.[6] These experiments measured the response of blood pressure in laboratory animals to infusion of exogenous angiotensin I before and after teprotide administration. In control animals exogenous angiotensin I caused significant increases in blood pressure. In teprotide treated animals the pressor response to angiotensin I was reduced by as much as ninety per cent. Thus, inhibition of angiotension converting enzyme was associated with an antihypertensive effect. These findings were later duplicated in normotensive human volunteers.

In 1974 the effects of teprotide were studied in thirteen patients with hypertension.[7] Twelve of the thirteen patients had a reduction in blood pressure following bolus injection of teprotide. All of the patients with renovascular, malignant, or essential hypertension responded well, while two patients with chronic renal failure responded poorly. In five of the responders teprotide was again administered after the patient was salt depleted with a low salt diet and diuretics. Although reduction of both systolic and diastolic pressures was enhanced following salt depletion, the degree of blood pressure reduction did not correlate with control levels of renin activity.

In a larger study the effects of teprotide and saralasin were compared in 39 hypertensive patients on normal sodium diets.[8] All patients were classified according to control renin profiles as low, normal, or high renin hypertensives. Patients with low renin hypertension had no change in blood pressure with teprotide, but did have a rise in blood pressure saralasin, most likely due to the saralasin's partial angiotensin agonist properties. In contrast to the low renin group, patients with high renin hypertension responded well to both teprotide and saralasin, but had a significantly greater fall in blood pressure following teprotide. Of interest, the 23 patients with normal renin profiles had no response to saralasin but did sustain a significant reduction in blood pressure with teprotide.

These results confirmed those of the previous study; demonstrating that the enzyme inhibitor teprotide is an effective antihypertensive agent in patients with normal or high renin levels. Teprotide was superior to saralasin in both of these patient sub groups and did not induce a pressor response in the low renin patients. Unfortunately, like saralasin, teprotide has limited applicability because it must be given parenterally.

Captopril

The most recent advance in the development of the enzyme inhibitors has been the synthesis of Captopril (SQ14225), which can be taken orally.

Animal studies demonstrated that captopril had no effect on normotensive rats but did cause reductions of blood pressure in Goldblatt two kidney renal hypertensive rats and in some spontaneously hypertensive rats (SHR). SHR is currently the animal model most representative of essential hypertension in humans.

Shortly therafter it was shown that a single oral dose of captopril abolished the pressor response to exogenous angiotensin I in normal humans. In 1978 reports of therapy of human hypertension with captopril were published. In one study, twelve patients (6 with essential hypertension and 6 with renovascular hypertension) were treated with captopril for periods of 3 to 24 weeks.[9] Plasma levels of renin, aldosterone, and angiotensin converting enzyme were measured before and during therapy.

In both groups of patients plasma renin activity increased, while plasma converting enzyme, and plasma aldosterone decreased, indicating that the doses of captopril used (400 to 1000 mg) effectively reduced angiotensin II generation. Mean blood pressure in the patients with essential hypertension fell from 166/110 to 136/91 and blood pressure fell from 189/109 to 135/84 in the patients with renovascular hypertension. Control plasma renin activity ranged from 0.9 ng/ml/hr to 17.0 ng/ml/hr. There was no correlation between pretreatment plasma renin activity and fall in blood pressure with captopril - all patients sustained marked reductions in both systolic and diastolic pressure. Four of these patients had been refractory to prior medical therapy, yet they remained well controlled for as long as six months as outpatients while taking captopril.

These encouraging results are supported by a recent study of captopril therapy in 19 patients (13 with essential hypertension; 6 with renovascul hypertension).[10] Eighteen of the 19 patients beca normotensive (3 after chlorthalidone had been added captopril). All patients with normal or high ren profiles became normotensive. One of two low ren patients did not respond.

In these studies then, 30 of 31 patients with eith essential or renovascular hypertension have respond well to captopril. Responders included all of the patien with normal renin profiles. Control of hypertension w achieved without orthostatic hypotension, clinical apparent volume overload, central nervous syste depression, or fatigue and weakness. Three patien developed possible toxic or allergic reactions to captop characterized by fever and erythematous maculopapul skin rash occurring approximately one week aft beginning therapy. These signs cleared within sever days after the drug was withdrawn.

State of the Art

In summary, enzyme inhibitors are a promising ne class of compounds in the treatment of hypertensio Captopril (SQ14225) is effective when taken orall These agents not only decrease generation angiotensin II, but also decrease metabolism bradykinin. They therefore potentially have a dual mo of antihypertensive action -reduction of a circulati vasopressor and enhancement of a circulati vasodepressor.

Lack of correlation between response to therapy an pretreatment renin status indicates that reduce angiotensin II generation is not the sole mechanism action. The as yet limited data suggest broad utility the enzyme inhibitors in the treatment of most patien with essential hypertension, regardless of their reni status.

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Controversies
In Medicine

reatment of Children and dolescents with Radioiodine 31-I) for Hyperthyroidism

ichael Lawson, M.D.

Treatment of hyperthyroidism in children and dolescents is almost exclusively treatment of Graves' sease. The therapeutic goal is to establish and maintain eumetabolic state with therapy which is effective and oses acceptable risks to the patient and his family. hen this can be achieved with antithyroid medication ropylthiouracil or methimazol) without serious roblems in medical management or unacceptable drug eactions this is preferable to thyroid ablation with urgery or radioiodine. The Graves' disease may ventually remit and the patient may avoid thyroid estruction and attendant hypothrodism. yperthyroidism, however, is not a benign disease, and not controlled it can adversely affect a young person's hysical wellbeing and have detrimental and lasting ffects on his emotional, social and academic evelopment.

When thionmide drug therapy, fails for any reason, nd a decision is made to definitively treat the yperthyroidism both surgery and radioiodine (131-I) hould be considered in the context of the patient and amily's needs. Each treatment is effective if sufficient

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rom: Good Samaritan Hospital, 1033 E. McDowell Road, Phoenix, AZ 5006

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^{131}I Treatment of Hyperthyroidism in the Young Should it be used?

Sidney C. Werner, M.D.

Few now quarrel with the dose-limiting restrictions imposed by the National Council on Radiation Protection[1] to minimize radiation exposure from non-medical, and medical diagnostic sources. Its International Protection counterpart is cited as stating there is no threshold to radiation effect so that "all unnecessary radiation exposure should be eliminated," although others feel the issue is not closed. Nevertheless, radiation is both carcinogenic and mutagenic in man, as well as productive of chromosome breakage. The former has been recently popularized by way of the increased prevalence of thyroid cancer which has followed inadvertent radiation exposure in infancy and youth.

From: University of Arizona, Health Sciences Center, Dept. of Internal Medicine, Tucson, AZ 85724 and 1601 N. Tucson Blvd., Tucson AZ 85716.

thyroid tissue is destroyed and both are irrevocable. With either treatment life long medical follow-up is required with eventual thyroid hormone replacement expected. Neither treatment should be considered safe although the risks of each are quite different.

Surgical complications,[1] while infrequent with experienced thyroid surgeons, do occur and are not trivial. If too little tissue is removed the incidence of recurrent hyperthyroidism increases, a situation which usually requires subsequent radioiodine (131-I) therapy since surgeons are reluctant to operate a second time. As greater amounts of thyroid tissue are removed the surgical risk is bound to increase. The risks include those of intubation and anesthesia in addition to airway obstruction from aspiration or a rapidly forming hematoma, injury to the recurrent and superior laryngeal nerves and hypoparathyroidism.[2] A thyroidectomy scar is a necessary concommitant of surgery as is the expense of surgery and hospitalization.

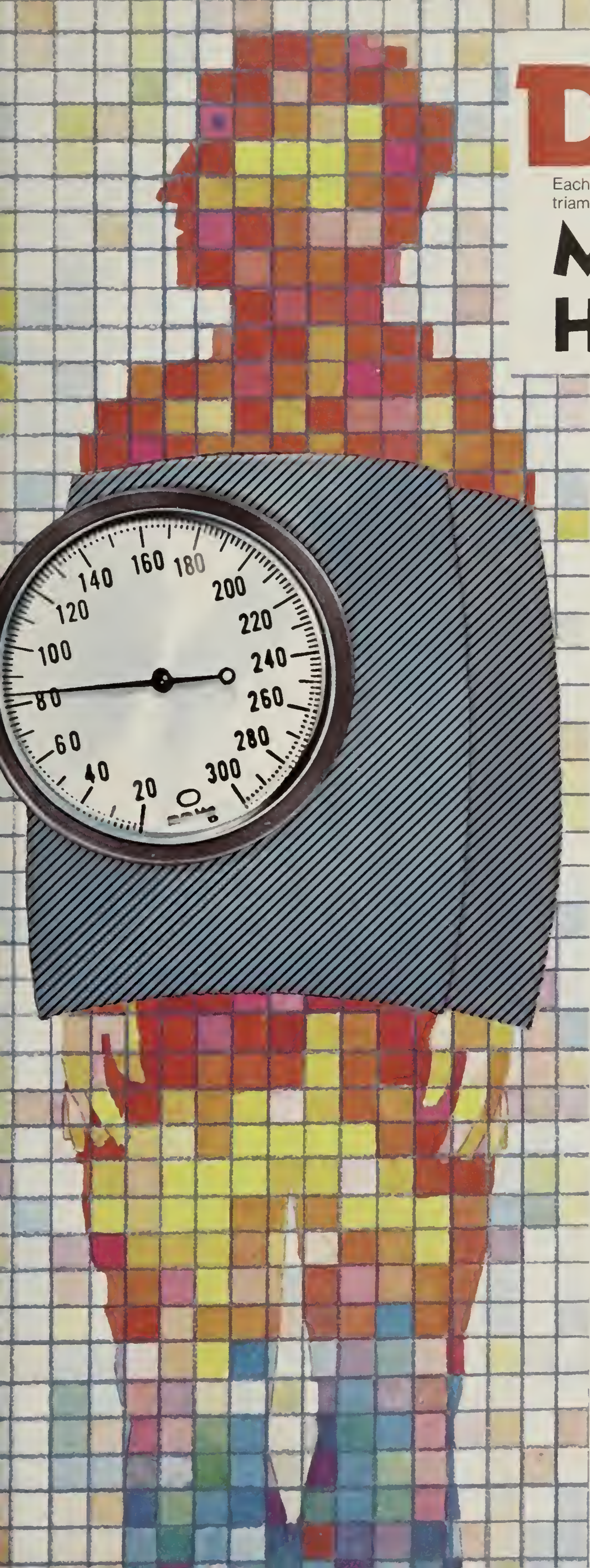
Radioiodine (131-I) therapy, the treatment of choice in most adults, is easy to administer, can be given to outpatients and is relatively inexpensive. Children and adolescents, however, have a greater life expectancy than adults, have potential procreative capacity and are clearly more at risk from the ionizing effects of radiation. There exists a legitimate concern that radioiodine therapy could induce thyroid neoplasia, leukemia or cause significant genetic injury leading to increased fetal wastage and congenital abnormalities in offspring. An association between thyroid irradiation and neoplasia has been established under different circumstances with radiation of the scalp,[3] thymus,[4] neck and chest[5] and in association with nuclear explosions with exposure to the populations of Hiroshima and Nagasaki in 1945[7] and the Marshall Islanders in 1954.[8] The calculated doses ranged from 6.5 to approximately 1,500 rads. These radiation induced thyroid cancers have been discovered as late as 40 years following exposure.[9] Dobyns et al[10] failed to demonstrate an increased incidence of thyroid nodularity or cancer in 19,000 patients treated with therapeutic doses of radioiodine (131-I) in the range of ±10,000 rads compared to patients treated surgically. There were 322 patients under the age of 20 in this series. The cooperative study did, however, indicate a lower frequency of nodularity and neoplasia in those patients who became promptly hypothyroid and were placed on thyroid hormone compared to those patients who became euthyroid and received no supplemental thyroid hormone. These data suggest that higher doses are more apt to destroy the replicative function of thyroid cells leading to hypothyroidism but not inducing malignancy. Safa et al[11] recently reported experience with a radioiodine (131-I) treated group of children and adolescents followed for 5 to 24 years finding no thyroid cancers, no leukemia and no increased incidence of fetal

Despite the response to these considerations in diagnostic usage of radioisotopes[2] or x-ray examination, ^{131}I in millicurie amounts is being strongly recommended as the way to treat hyperthyroid children, and young adults in the childbearing era. True, the resultant exposure to radiation is within the margin specifically allowed for medical purposes. But if there are alternative methods of therapy, why use up radiation tolerance early in life. Loss of radiation tolerance may be regretted should later exposure to large radiation doses occur, possibly, due to accident, war, or need for high dose radiotherapy upon onset of a life-threatening disease. In addition, why risk polluting the human genetic pool in future generations, through a cumulative increase in number of mutations resulting from gonadal radiation consequent to I therapy, however small or large the increase may be interpreted as being.[3, 4]

Induction of mutations following radiation exposure of the gonads is not an isolated event. We live surrounded by other environmental mutagens and carcinogens than radiation, as any of the recent volumes of Mutation Research will attest.[5] These may possibly be additive to the effects of radiation. The same applies to carcinogenesis. Thus, knowledge of the effect of whole body exposure to low radiation doses (with or without added evironmental mutagen effects) could now be in the same stage as before radiation of the thyroid in infancy and youth during treatment for thymus or tonsil enlargement was correlated with later increased prevalence of thyroid carcinoma.

Several recent calculations have been made of the increase in mutation rate to be expected from concurrent ovarian (or testis) radiation during ^{131}I therapy of hyperthyroidism, as a consequence of circulating sodium ^{131}I and ^{131}I labeled thyroid hormones and of radioactivity from bladder urine. Such figures are open to a wide range of variability. For example, the calculated rad dose to the ovaries has varied from 0.05 to 5.37 rads mCi. Nevertheless, in two latest estimates, the increase over background birth defects has been calculated to be 0.6% in one[3] and 0.4% in the other.[4] As the first authors state, the figures are "small or large" depending on the point of view. Dr. Edith Quimby has repeatedly stated[6] "whereas such figures mean little for the immediate progeny of the patient, they have significant implications for the genetic pool of future generations, particularly when two ^{131}I treated parents mate."

There are two effective alternative treatment modalities, surgery and chronic antithyroid drug therapy. The choice of surgery presupposes a surgeon trained in thyroid surgery who does these operations frequently. In one series, 3774 patients underwent subtotal thyroidectomy for hyperthyroidism with no mortality or serious morbidity.[7] Late hypothyroidism increased cumulatively during the 1960's, but is



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Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K+ frequently; both can cause K+ retention and elevated serum K+. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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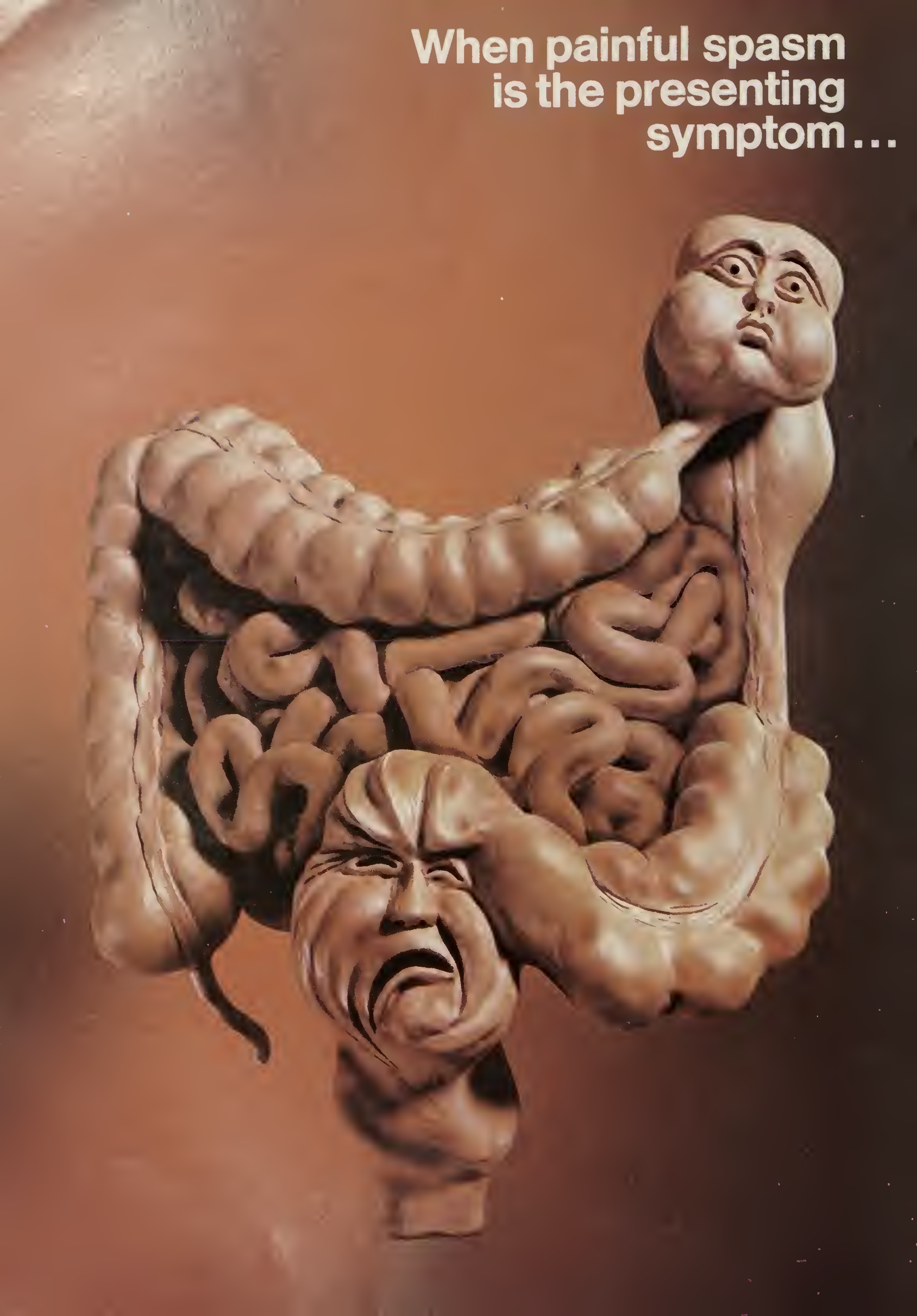
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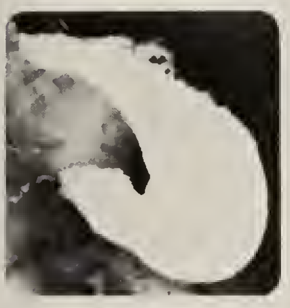
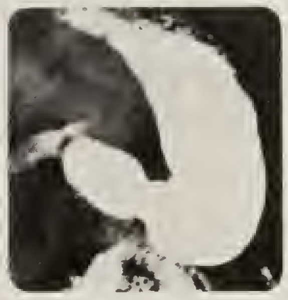
. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



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*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:
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Do not rely on the use of the drug in the presence of complication of biliary tract disease Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate With overdosage, a curare-like action may occur ADVERSE REACTIONS Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention; blurred vision and tachycardia, palpitations; mydriasis; cycloplegia, increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia, nausea; vomiting, impotence; suppression of lactation, constipation; bloated feeling, severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation DOSAGE AND ADMINISTRATION Dosage must be adjusted to individual patient's needs

Usual Dosage Bentyl 10 mg. capsule and syrup. *Adults* 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children* 1 capsule or teaspoonful syrup three or four times daily. *Infants:* ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg: *Adults* 1 tablet three or four times daily Bentyl Injection: *Adults* 2 ml. (20 mg.) every four to six hours intramuscularly only NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE: The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.

Product Information as of October, 1978.

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wastage or congenital malformations in the progeny of treated patients from that of the general population. These latter findings are not surpising since the gonadal and whole body doses are sufficiently low approximatley 0.4 rads/mCi.) so that one would not expect to see a statistically significant increase of leukemia or genetic injury in groups of the size studied to date. The risk is theoretically present but statistically small as in the case of all diagnostic radiologic procedures performed on children and adolescents.

Radioiodine (131-I) treatment of adolescents or children with Graves' disease is indicated when surgery is unacceptable to the patient or family, when hyperthyroidism has recurred following surgery, when there are underlying medical conditions which inhance the surgical risk and when access to a skilled thyroid surgeon is not available. The increased cost of surgical therapy must also be factored into the choice equation. 131-I therapy should neither be considered safe nor the treatment of initial choice for hyperthyroidism in children and adolescents. It's use is occasionally warranted and the theoretical risks of the radiation should be considered in conjunction with the surgical risks and in the overall context of what is in the best interest of the patients and his family.

It is my opinion that when definitive therapy is necessary, regardless of whether surgical or radioiodine treatment is selected, there should be a commitment to thyroid ablation and lifelong thyroid hormone replacement. This course of action should spare the patient the combined risks of surgery and radiation exposure and should reduce the subsequent incidence of thyroid nodularity and neoplasia.

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currently waning as less agressive procedures are being performed.[8]

Chronic antithyroid drug therapy in children has not resulted in permanent remission in most instances, in my personal experience. In this series,[9] the children were maintained euthyroid on drug until age 16½-17 or so, when surgery was able to be perfomed with the same excellent outcome seen in the adult, and unlike the poor results of such surgery at a younger age. Serious side effects of chronic drug therapy were not seen, nor was lack of compliance a problem, though awareness of these is essential.

In conclusion, the reasoning above suggests to this author that if competent surgery is available, or when chronic antithyroid therapy is practical, or both as indicated above, these be employed in preference to radioiodine in the treatment of hyperthroidism in children and adults in the childbearing era.

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Editorials

"It Must be Emotional": The worst words In Medical Practice

A thread which seems to run through almost all medical practices is that most patients have emotional components to their medical problems. Some, in fact, have only the former and have been aptly called the "worried well." For the uninitiated, it is extremely difficult to learn how to deal with these kinds of patients. To help shed some light on the problem I undertook an informal biased survey of several established clinicians to gain some insight into how they deal with this problem.

Clearly, the most prevalent approach appears to be to ingore emotional problems in patients. Most physicians queried simply do not discuss the possibility that the patient's symptoms could have an underlying emotional basis. Rather, they allow the patients to ventilate, offer minimal support and then supply a pharmacological agent to tide the patient over the acute stressful situation. The physicians state that the patients usually overcome the acute stressful situation on their own and there is no need for the doctor to spend a great de
of time with them discussing th
problems. The major drawback to th
approach voiced by some physician is th
over the long haul these patients ha
constant stresses which produc
intermittently debilitating sympto
necessitating more than transie
medication. Thus, many such patients a
on daily drugs which lead to additio
This is especially prevalent for t
"minor" tranquilizers.

Another approach, favored by so
physicians, is a thorough search for a
underlying physical cause for t
patient's symptoms. Philosophically, th
is a justifiable approach for it enables t
physician to "make certain" that there
nothing wrong with the patient
account for the symptoms. This approa
leads to much testing with biochemic
and radiological techniques. The patie
is given some hope that somethi
physical will be found which will requi
medical treatment. In the vast majority
such instances, however, nothin
abnormal turns up and the doctor a
patient must then face the cruci
question of "what's causing m
symptoms, Doc?" Most physicians in th
category tend to again deny t
underlying emotional nature of t
patient's complaints to some extent a
prefer to tell the patient that they tru
believe their symptoms are real but th

nnot localize the underlying cause for e patient's difficulty. "Perhaps with ne the underlying physical ailment will ar its 'ugle head' and the cause will be posed" is a common refrain. Usually the ıal recommendation by such physicians to return in three to six months to assess the situation. Again, in the terim, minor tranquilizers or other ychotrophic drugs such as pain edications, some with narcotics, are escriabed for minor complaints ranging om headaches to gastrointestinal mptoms.

Lastly, an approach which was favored very few physicians was one of "free scussion." According to these ysicians it takes usually five minutes to a consultation to assess whether ere truly is an underlying organic oblem or whether the patient has edominantly emotional complaints. ese physicians approach the patient at e onset with the possibility that no ganic physical disease will be found but at there probably is an emotional mponent to their symptomatology. A ysical as well as emotional evaluation is dertaken simultaneously in an attempt deal with both possibilities. Since no cision can be made regarding an derlying physical problem so early in e course of evaluation, no medications e prescribed for "we would not know hat we are treating." If nothing turns up physical evaluation, then the patient is ready ensconced in an emotional ogram which hopefully will produce sitive results and alleviate the mptomatology. As a rule, medications e usually not prescribed by the medical ysicians but they are left to the scretion of the emotional consultant.

These markedly different approaches the same problem reflect to some gree the underlying pinnings of the ysician.

hose comfortable discussing and obing the problems of their patients ill no doubt use the last approach while ose who feel ill at ease or ill equipped to so would probably use the first proach. It's not clear to me which ethod is the best or even if one is good the time. Perhaps, judicious use of all ree methods would be the most dvantageous path to follow. I guess the ey point is that we should be using *all ree approaches*, not just one to exclusion. I ave a feeling that the "denial" approach as been overutilized. Greater utilization f "free-discussion" with our patients will ield greater rewards both for our atients as well as ourselves as hysicians.

arshall B. Block, M.D.
ditor

Non-Physician Patient Instructors

A physician's skills in medical interviewing and physical diagnosis form the cornerstone of patient care and are integral to the art of medicine. The acquisition of complete and accurate data is crucial to clinical decision making and the provision of quality patient care. Until recently, there have been few objective and reliable methods to evaluate these critical skills. Instead, assessment of clinical performance has often rested on subjective criteria and errors in data collection have gone unnoticed.

When a student or resident obtains a medical history from a patient, how can an attending physician guarantee that all relevant data has been obtained unless the attending likewise obtains a complete history? How can an examiner's interviewing skills, questioning style, or the rapport developed with the patient be critiqued unless an attending physician is a silent observer of the interaction?

Similar problems exist for the physical examination. How can an attending physician evaluate whether an examiner is exerting sufficient pressure in the palpation of the flanks so that an abnormality deep in the abdomen could be detected if one were present? If an examiner is observed auscultating the heart, only the placement of the stethoscope on the correct locations on the chest wall and the use of both the bell and diaphragm can be noted. The accuracy of the description of the patient's findings can only be ascertained if the observer likewise performs a cardiac examination on the patient.

In an effort to solve some of the problems involved with the reliability evaluation of data collection skills, faculty at the University of Arizona College of Medicine have implemented an innovative program which employs highly trained non-physician patient instructors who function as patients, teachers, and evaluators of these fundamental skills. The patient instructors first serve as patients and are interviewed and examined. Following the examination, the patient instructors assume the role of teacher and evaluator and critique the examiner's performance according to pre-established guidelines. Maneuvers omitted or performed incorrectly are reviewed; physical findings which are identified or described inaccurately are discussed. The patient instructors provide feedback to the examiner on interviewing style and suggest methods to enlist patient cooperation and elicit complete information. Symptomatic patient instructors with stable positive findings on physical examination question the examiner on what was detected while examining the heart, lungs, or joints and then confirm or deny those findings. The examiner is given the opportunity to repeat those segments of the examination performed inadequately or described incorrectly. Thus the patient instructors should be regarded as highly trained teachers and evaluators who use themselves as teaching material.

For each examination, objective and validated checklists have been developed. The checklists include items dealing with the doctor-patient relationship and the completeness of the examination or interview. In addition, they provide an opportunity for the examiner to record and describe findings. The scoring of these checklists has been studied and shown to be statistically reliable and reproducible.

Patient instructors have been trained by physicians to teach and evaluate a pediatric and an adult medical history, a complete examination of an asymptomatic adult, a screening neurological examination of an asymptomatic adult, the cardiovascular examination of patients with heart murmurs, the pulmonary examination of patients with asthma and bronchiectasis, the musculoskeletal examination of patients with arthritis, and the neurological examination of patients with multiple sclerosis.

There are many other areas in which this technique is applicable. Ophthalmologists at the College of Medicine are training patient instructors to evaluate students' ability to identify and describe retinal lesions. Patients with chronic leukemia and no immediate need for therapy can be used to teach the examination of liver, spleen, and lymph nodes.

Patient instructors are being used to teach and evaluate the skills of second and third year medical students, first year internal medicine and family practice residents, and nurse practitioner students. A future goal is to utilize patient instructors as part of a comprehensive program for certification, recertification, and continuing medical education.

All of the faculty at the College of Medicine who are involved with this program are excited about its potential. The patient instructors provide a method to evaluate aspects of medicine that were previously considered an art and not subject to rigorous scrutiny.

Paula L. Stillman, M.D.
Coordinator, Preparation
for Clinical Medicine
Associate Professor, Pediatrics
Louis J. Kettel, M.D., Dean
College of Medicine
University of Arizona

Auxiliary Highlights

Bylaws being what they are, usefulness is measured in part by the degree of current status. A champion few people become involved in bylaws review and overhaul in their lifetimes, and Mrs. Joseph (Maude) Reno is now leading the troops through updating the Auxiliary Bylaws. Alert to correlation of changes in National bylaws, three proposed changes of significance will be considered at the Annual Meeting. Included is a possible formula modification for naming members to the nominating committee and would qualify a second member from counties with over 300 members. Long Range Planning would be added to standing committees, and Auxiliary membership catagories would be expanded to include spouses of interns, residents, and medical students.

Other business presented at the February board meeting provided enthusiastic reporting of the presidents-elect who attended the Chicago Confluence and returned with tales of noteworthy ideas and motivation to be reflected in the coming year's activity as presidencies are assumed and the value of the traditionally well planned confluence is demonstrated through local translation.

Selma Targovnick, M.D., ArMA legislation chairperson, spoke to Auxiliary members concerning abortion, podiatrists, legislative mandates, medical records ownership, homeopathic physicians, certificates of need for office locations, and numerous other subjects sometimes infected by legislative proponants. Dr. Targovnick confirmed the effectiveness of legislative contact and the importance of additional campaign support money to encourage availability of listening ears when necessary. ArMPAC provides a direc contributions avenue for Arizona doctors and spouses to help maintain active vigilance.

Continuance of printing Health Career Education reference charts for students came into focus for review of need, cost format and utilization. Their usefulness is generally lauded and many thousands have been provided to schools for years, but economy is prompting further evaluation.

The Health System Agency under which state Coordinating Councils are reported working in 200 areas of the country are involved in health planning partly due to health costs. Controlling costs through controlled planning is the name of the game, but how it's played depends largely upon who's on the team. Input from physicians is lacking unless deliberately arranged. Council membership is restricted, but meetings are open and should be attended so efforts of the planners can be balanced if necessary for appropriate delivery. Spouses can help by attending meetings to keep in contact and gather information. Physicians and their societies are urged to work with the planners rather than fight the results of meetings not attended and also meet with the task force if possible.

A recent Direct Line Newsletter reported a Lou Harris poll indicating that patients are highly influenced by their doctors but claim that they are not being advised on weight loss, smoking and exercise. (Wonder how many shoes are out there having fits.)

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In Memoriam

David C. H. Sun, M.D.
1922—1979

David, who preferred to be called "Dave" by his friends, would probably entitle this presentation *"David C. H. Sun, M.D., The Man, The Physician, and The Friend."* David Sun, *The Man*, was born in Haugchow, China in 1922, son of Kya Foh and Wing Chow Sun. He earned his undergraduate and medical degrees in Shanghai. He came to this country in 1946, to learn his specialty in Gastroenterology at the University of Pennsylvainia under Dr. Henry Backus. Not surprisingly, the student soon began to emulate and equal the reputation of his great teacher.

In 1947, he married Jeanise Chen, whom we all know, cherish, and love. Jeanise, in her own right a well known biochemist, was even more importantly to David a most devoted and loving wife, as well as adviser and companion.

In 1962, Dave adopted this beautiful country of ours, became a citizen, and has been one of the most devout Americans that I have ever known. And yet, he never forgot his native country and was always proud of his heritage.

David Sun, *The Physician* has earned, and rightfully so, a preeminent positon as one of the world authorities in Gastroenterology of the present time. He has published 85 articles, one text book, two monographs and numerous chapters in textbooks of Gastroenterology. He has traveled the world to speak at seminars, many of which he had helped to organize. Perhaps as a result of this, his private practice has been universal in scope, from the lowest peons to the richest potentates of the East. He demanded and received from his patients the devotion to the adminstrations of a dedicated man; but he never demanded any more of them than he demanded of himself in his practice of medicine!

From 1960 to 1965, David, *The Physician*, was Director of Research and Education for the entire Veterans Administration in Washington, D.C., as well as holding professional rank at George Washington University.

In 1966, he moved his entire research staff to the Vetrans Administration Hospital in Phoenix and continued his research activites in Gastroenterology locally.

in 1967, David, *The Physician*, setup the first specialized laboratory at a local hospital and established the Institute of Gastroenterology at the same hospital. He also developed a fellowship program for the training of young Gastroenterologists. These were all "firsts" in the State of Arizona.

Shortly after his arrival in Phoenix, he initiated Gastroenterology seminars for the dissemination of the most recent advances in his specialty. Because of his own great reputation and standing, he was able to obtain the most prominent men in the specialty as speakers, such as Dr. Henry Backus, Dr. Joseph Kirsner of the University of Chicago, and others in all fields pertaining to Gastroenterology. The names are to numerous to recount here.

Despite the fact that he knew of the sword hanging over his head, he planned ahead. In fact, it was during a planning session for the Seminar in 1980, that he suffered his catastrophy.

Undobtedly, his influence in upgrading the practice of Gastroenterology will be felt for many years to come, both locally, nationally, and internationally.

I first became acquainted with Dave, *The Friend*, in 1967, and had the greatest of good fortune to develop, early on, a close personal friendship with this man.

In that year, he set up his office for the private practice of Gastroenterology in the same office building in which I was located. He did this in order to apply his academic knowledge for the benefit of private patients, which as mentioned before, became most protean and catholic in scope.

Periodically, he would visit with me and talk about many things. This custom was not confined to myself alone, but to others in the building — and, we always looked forward to these visits.

He would concern himself with family, medicine, particular patients, social events in which he was an active civic participant, and always an intriguing variety of subjects.

He was always kindly, considerate, courteous, and perceptive, and always the gentle, soft-spoken Chinese-*American* that he was. Not once did I know him to raise his voice in anger, or against any member of his profession, his friends or acquaintences.

And he did enjoy a good laugh! His laughter and good sense of humor were infectious and contageous.

No one enjoyed his friends more than Dave Sun. He loved to entertain, did so frequently, and no one enjoyed his parties any more than the host himself.

It is tragic that this man should have been taken from us at this stage in his life. For, he was at the apogee of academic and professional achievement, and still growing and planning ahead. But — it is so, and we must all accept it with good grace.

David Sun, you will long be in our hearts and thoughts.

David James, M.D.

ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

GOVERNMENTAL SERVICES

Meeting of the Governmental Services Committee of the Arizona Medical Association, Inc. held at 810 West Bethany Home Rd., Phoenix, Arizona on Wednesday, January 10, 1979, convened at 7:00 p.m., Louis C Kossuth, M.D., Chairman presiding.

REPORT OF THE CHAIRMAN

CAHSA Annual Meeting

Dr. Kossuth discussed the CAHSA Annual Meeting held November 29, 1978. He informed the committee that he made a motion at that meeting that: The President of CAHSA, within 30 days, appoint a committee to prepare proposed amendments to the CAHSA bylaws. Further, that such proposed amendment provide for 1) the impeachment process; 2) reasons for impeachment proceedings that shall include concealment of information from the public including CAHSA Board of Directors, and such other actions that the Committee desires; and 3) the termination of employment of any staff member that conceals information from the public including the CAHSA Board of Directors. The motion was passed. RECEIVED FOR INFORMATION.

Productivity Standards - Califano

Dr. Kossuth provided the Committee with an article from *U.S. Medicine*, November 15, 1978, "Standards to Judge Productivity Slated," in which Joseph A. Califano, Jr. presents his plans to set standards for evaluation productivity of the health care sector, including physicians. Dr. Kossuth pointed out that the critical aspect will be the criteria to measure efficiency, effectiveness, and quality. RECEIVED FOR INFORMATION.

Understanding the Health Care System

Dr. Kossuth discussed his letter to the Committee (November 6, 1978) relative to the SHCC training session on October 27. The highlights of the training session were the discussion of cost containment, National Health Insurance, and the manpwoer problem. RECEIVED FOR INFORMATION.

Cost Containment

Dr. Kossuth discussed his letter to the Committee of November 9, 1978, in which he reviewed his recent activities as a member of the SHCC Health Resources Development and Review Committee with regard to cost containment.

RECEIVED FOR INFORMATION.

Nursing Care Institutions Regulations

Dr. Kossuth provided the Committee with an outline of a presentation he made at a public hearing with regard to the proposed regulations for nursing care institutions. He pointed out that implementation of these regulations would not be cost-effective. It was announced that due to the criticism of the proposed regulations by many, Dr. Dandoy would probably scrap the current proposal and start over. RECEIVED FOR INFORMATION.

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"Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis

Final classification of the less-than-effective indications requires further investigation.

Contraindications: Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.**

As with all anticholinergics, inhibition of lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship not established.

Adverse Reactions: No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated, avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

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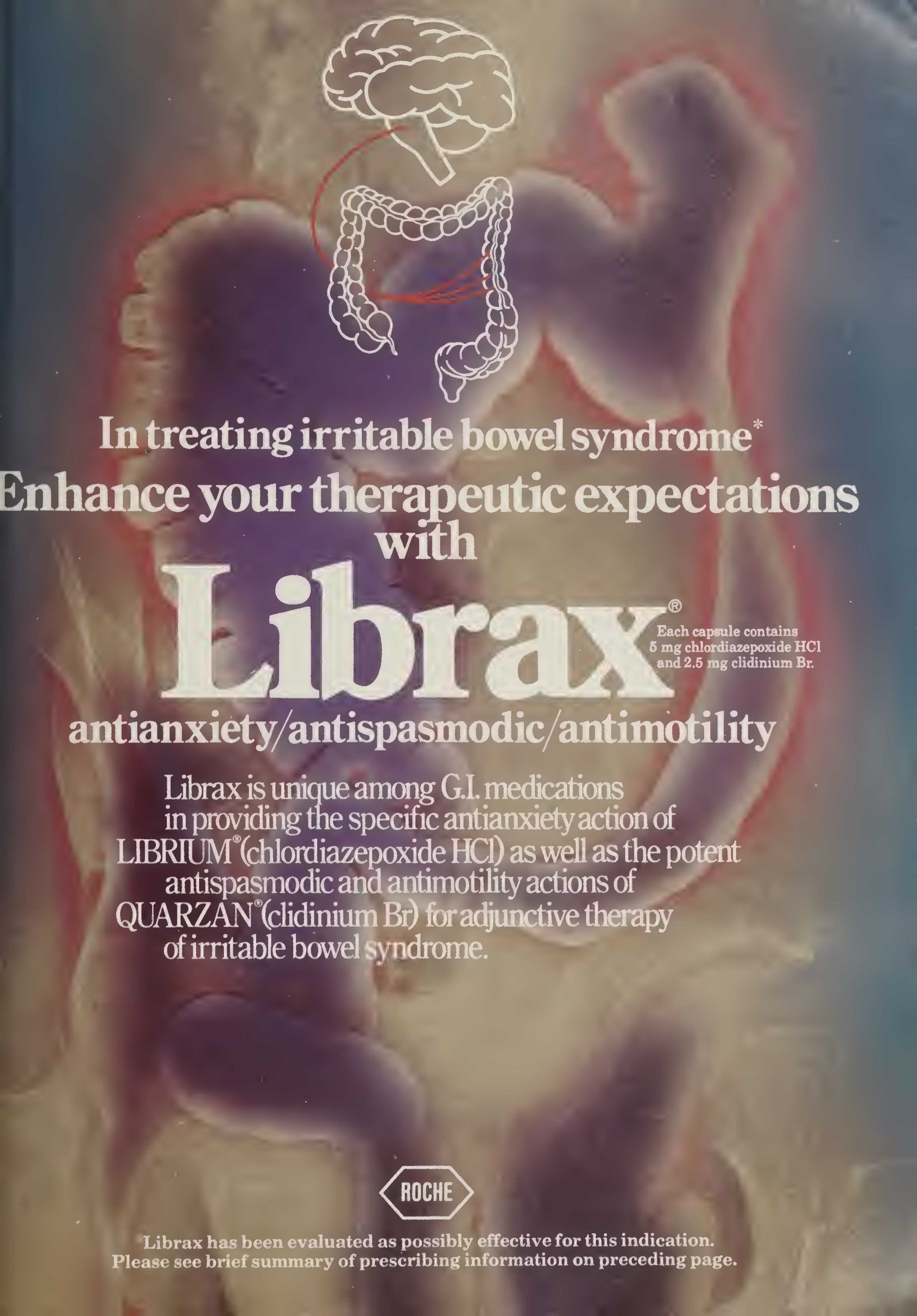

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Please see brief summary of prescribing information on preceding page.

The evidence of experience

Since October 1974 when Motrin® (ibuprofen) was introduced in the United States, it has been used by more than 6,000,000 patients with rheumatoid arthritis* or osteoarthritis. Rarely has an ethical pharmaceutical product been prescribed for so many patients in so short a time. In addition, more than 450 studies presenting new data related to Motrin have been published.

The 6,000,000 patients already treated with Motrin is an objective measure of physicians' confidence in the ability of Motrin to relieve the pain and inflammation associated with rheumatoid arthritis and osteoarthritis.

So it is not surprising that in this short period Motrin has become the most frequently prescribed alternative to aspirin. Motrin relieves joint pain and inflammation as effectively as indomethacin or aspirin, but causes significantly fewer CNS and milder GI reactions. However, gastrointestinal bleeding, sometimes severe, has been associated with Motrin, aspirin, indomethacin, and other nonsteroidal antiarthritic agents.

*The safety and effectiveness of Motrin have not been established in patients with Functional Class IV rheumatoid arthritis (incapacitated, largely or wholly bedridden, or confined to wheelchair; little or no self-care).

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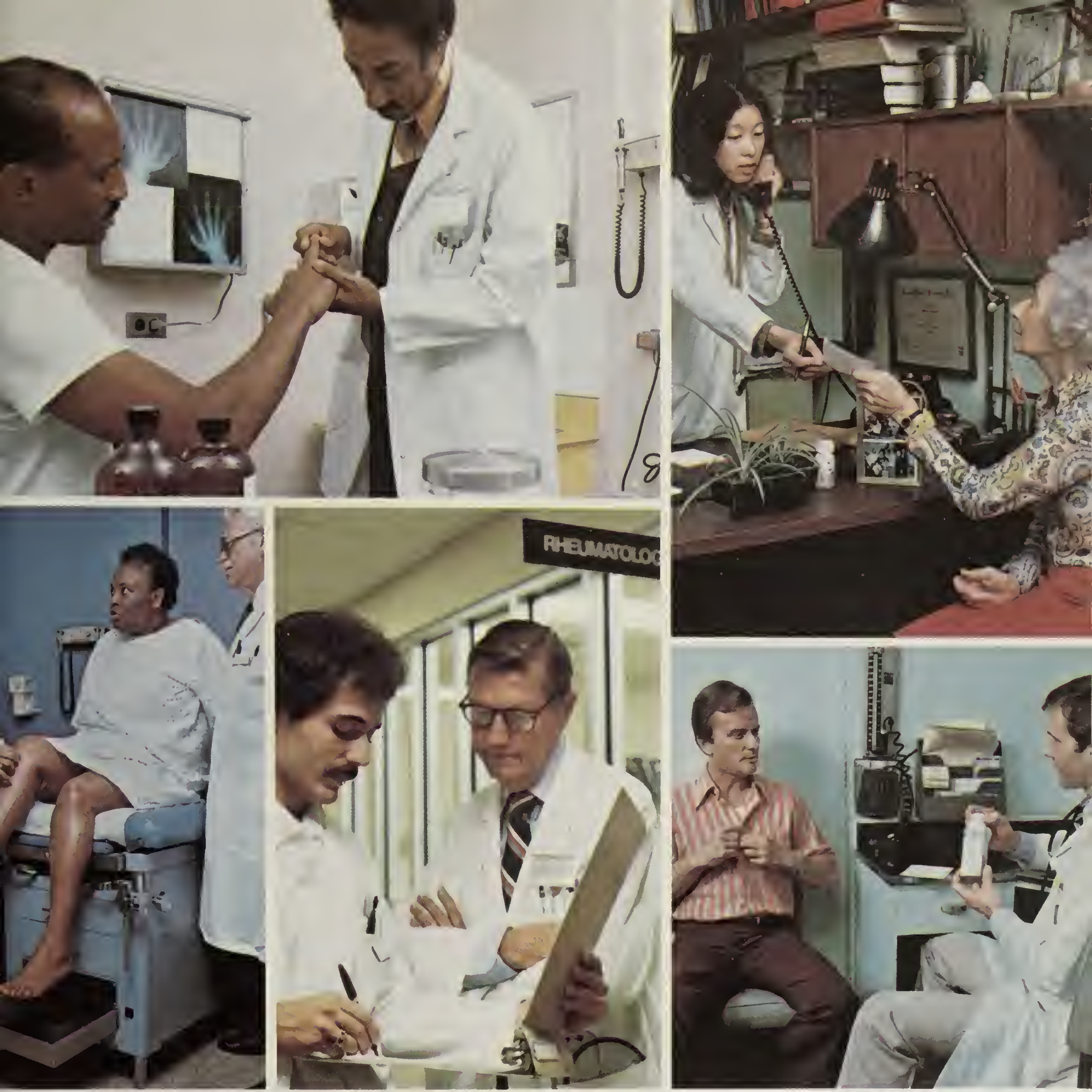

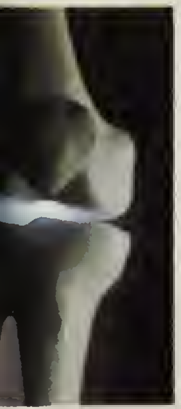

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Motrin 400 TABLETS mg
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Indications and Usage: Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Contraindications: Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

Warnings: Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.

Drug interactions. *Aspirin* used concomitantly may decrease Motrin blood levels. *Coumarin:* Bleeding has been reported in patients taking Motrin and coumarin.

Pregnancy and nursing mothers: Motrin should not be taken during pregnancy or by nursing mothers.

Adverse Reactions

Incidence greater than 1%

Gastrointestinal: The most frequent type of adverse reaction occurring with Motrin (ibuprofen) is gastrointestinal (4% to 16%). This includes nausea*, epigastric pain*, heartburn*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness*, headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

Incidence: Unmarked 1% to 3%; *3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

Overdosage: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

Dosage and Administration: Suggested dosage is 300 or 400 mg t.i.d. or q.i.d. Do not exceed 2400 mg per day.

How Supplied

Motrin Tablets, 300 mg (white)	
Bottles of 60	NDC 0009-0733-01
Bottles of 500	NDC 0009-0733-02
Motrin Tablets, 400 mg (orange)	
Bottles of 60	NDC 0009-0750-01
Bottles of 500	NDC 0009-0750-02
Unit-dose package of 100	NDC 0009-0750-06
Unit of Use bottles of 120	NDC 0009-0750-26

Caution: Federal law prohibits dispensing without prescription.

NIM-3

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001

Hospital Staff Organization - Placement of Nursing and Dietary Service

)r. Kossuth noted that the Department of ealth Services is proposing new regulations or hospitals in which nursing and dietary ervices personnel report to the dministrator. There was discussion as to hether these personnel should not more ppropriately report to the chief of the medical aff. If a State agency is attempting to dictate e chain of command in a hospital, this may be concern to the Association.

T WAS MOVED AND CARRIED THAT ROPOSED REGULATIONS AFFECTING MEDICAL CARE BY ANY STATE AGENCY E CAREFULLY REVIEWED AND THAT MATTERS IN THOSE REGULATIONS HAT MIGHT PRESCRIBE STAFF ELATIONSHIPS WITHIN THE HOSPITAL WILL BE OBJECTED TO ON THE ROUNDS THAT THIS IS A MATTER OF DECISION BY THE GOVERNING BODY OF HE HOSPITAL CONCERNED.

National Health Insurance

)r. Kossuth presented several articles oncerning the current views on National ealth Insurance. Resolution 62 (I-78) from he American Medical Association House of Delegates was received by the Committee and iscussed. It was the general consensus that rMA should re-evaluate its postion on Naitonal Health Insurance. Therefore, the ollowing resolution was drafted (modeled fter the AMA resolution) for consideration.

Whereas, It is a recognized fact that mericans have the best medical care system in the world today, and most polls indicate the ublic is generally satisfied with both the uality and quantity of medical services; and

Whereas, The polls have consistently eflected that the American people hold their ndividual physicians in higher regard and rust than any other professional; and

Whereas, It is this very personal doctor-patient relationship that will be dismantled and ltimately destroyed by national health nsurance if the freedom of the patient to hoose his system of health care is not rotected;and

Whereas, There is always an obligation to mprove any system; therefore be it

RESOLVED, That the Arizona Medical ecommend to the Congress of the United tates of America modifications to our present ealth care system embodying the following rinciples:

1. Requiring minimum standards to dequate benefits in all health insurance olicies sold in the United States with ppropriate deductible and co-insurance.
2. It is the responsibility of the state nd/or local governments to provide medically or those indivuals who are unfortunate nough (through no fault of their own, i.e., ge, disability, financial hardship, etc.) not to e able to provide for their own medical care.
3. A nationwide program by the private nsurance industry of America (and overnment if necessary for reinsurance) to make available catastrophic insurance overage for those illnesses and individuals where the economic impact of a catastrophic llness could be tragic. All catastrophic overage should have an appropriate deductible and co-insurance to make it conomically feasible and to avoid abuse.
4. A program developed pursuant to these principles should be adminstered at the state level with national standardization through federal guidelines assuring the patient the right to choose their own system of medical care.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ABOVE RESOLUTION BE INTRODUCED TO THE ARIZONA MEDICAL ASSOCIATION'S HOUSE OF DELEGATES, 1979 ANNUAL MEETING.

Definition of Provider and Consumer

Dr. Kossuth circulated a memorandum (January 2, 1979) in which he points out the difficulties inherent in the definitions established in P.L.39-641 as they relate to provider, indirect provider, and consumer. Indirect providers replace providers on Boards of HSA's. These terms, as interpreted by HEW could mean any member of a board of a private non-profit corporation or other organization that makes health policy could be considered an indirect provider. This could include all elected officials, and even a chief of police or fire department if they offered first aid services. Dr. Kossuth's memorandum is on file.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS OF THE ARIZONA MEDICAL ASSOCIATION TO RECOMMEND TO THE AMERICAN MEDICAL ASSOCIATION AND THE ARIZONA CONGRESSIONAL DELEGATION THAT SECTION 1631 (3) (B) (1) WHICH IS THE REFERENCE TO "FIDUCIARY POSITON" BE REPEALED.

What Language Do We Speak

"A Discursive Dictionary of Health Care" was developed by Lee S. Hyde, M.D. In 1974 for use during the 1974 debate over the various bills that became P.L 93-641. Since certain terms are subject to varied definitions by varied HSA's and SHCC, this dictionary would be useful in standardizing such terms.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATION RECOMMEND TO THE ARIZONA HSA'S AND OTHER GOVERNMENTAL AND QUASI-GOVERNMENT ORGANIZATIONS THAT THEY ADOPT THE DICTIONARY "A DISCURSIVE DICTIONARY OF HEALTH CARE" AND FURTHER, RECOMMEND TO THE AMERICAN MEDICAL ASSOCIATION THAT THIS DICTIONARY BE MADE THE REFERENCE DOCUEMENT FOR P.L. 93-641.

PROFESSIONAL COMMITTEE

Meeting of the Professional Committee of the Arizona Medical Association, Inc., held at 810 West Bethany Home Road, Phoenix, Arizona, on Tuesday, January 16, 1979, convened at 6:53 p.m., Joseph W. Hanss, Jr., M.D., Chairman, presiding.

SECTION ON MENTAL HEALTH AND SUBSTANCE ABUSE

Paul M. Bindelglas, Chairman of the Section, reported that the Arizona Recovery Centers Association is a broad-based alcoholism treatment and prevention umbrella serving the entire Valley area. Their stated goal is to serve the community with its diversity of alcohol problems and people. They try to draw on the resources at hand and to work in coordination with other cummunity services. ARCA has requested some affiliation with the Arizona Medical Association, however, in exactly what capacity has not been made clear. Dr. Bindelglas will pursue this matter further.

IT WAS MOVED AND CARRIED TO TABLE THE SUBJECT OF AN AFFILIATION WITH THE ARIZONA RECOVERY CENTERS ASSOCIATION.

SECTION ON SPORTS MEDICINE

5th Annual Sports Medicine Symposium

William C. Brainard, M.D., reported that the 5th Annual Sports Medicine Symposium will be held on Saturday, January 20, 1979. There has been a good response from coaches, trainers, student trainers and school nurses and administrators. There will be noted speakers from around the country. RECEIVED FOR INFORMATION.

Certified Athletic Trainers

The Athletic Trainers Association was organized in the Fall, 1978, to gain recognition for Athletic Training as a profession. They have asked to have a member of their Association appointed to the Professional Committee Section on Sports Medicine. RECEIVED FOR INFORMATION.

Central Arizona Orthopedics Society

The Central Arizona Orthopedic Society states a concern about compulsory second opinion by insurance carriers. They are on record as opposing the concept of mandatory second opinion. It is suggested that the Arizona Medical Associaton go on record reaffirming the principle that "a physician should seek consultation upon request; in doubtful or difficult cases; or whenever it appears that the quality of medical service may be enhanced thereby." And further, requests that the Insurance Department require all third party payors to allow benefit for second opinions which are at the request of the patient. It is believed that this may be considered positive public relations for medicine in Arizona.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATION GO ON RECORD AS RECOMMENDING TO THE DEPARTMENT OF INSURANCE THAT HEALTH INSURANCE POLICIES WRITTEN WITHIN THE STATE MUST MAKE PROVISIONS FOR SECOND OPINIONS AT THE REQUEST OF THE PATIENT.

ADVISOR TO AUXILIARY

Immunization Council

John T. Clymer, M.D., Advisor to the Auxiliary, reported that immunization brochures and booklets are now being distributed to physicians' offices in other counties by Auxiliary members.

SECTION ON ALLIED MEDICAL GROUPS

Hospital Privileges for Podiatrists

Joseph A. DuPont, M.D., reported that Arizona hospitals should be encouraged to make by-law changes which would allow podiatrists to become members of their staffs. The Arizona Hospital Association is currently conducting a poll of Arizona hospitals and of the 39 responses they have received to date, 17 have podiatrists on staff and 6 have made the requested bylaw changes. It was noted that the podiatrists plan to introduce legislation which would mandate their being accepted as members of hospital medical staffs. RECEIVED FOR INFORMATION.

Optometry

The optometrists are proposing, through the State Health Plan for 1978-83, that there are enough people specializing in the care of the eye to take care of the State of Arizona. This could have the adverse effect of making ophthamologists appear secondary to optometrists. Dr. Moore of the Ophthamology Society is actively working on the plan and has sought Dr. DuPont's assistance. RECEIVED FOR INFORMATION ONLY.

SECTION ON AGING AND GENERAL MEDICINE

Definition of Death

Robert L. Hagan, M.D. reported that this Seciton is continuing to work on the development of a definition of death. They hope to have something for introduction during the annual meeting. RECEIVED FOR INFORMATION ONLY.

SECTION ON POISON CONTROL

Regional Poison Control Centers

Helen Johnson, M.D. explained the need of a regional poison control center in the state of Arizona. It is necessary that for the purpose of disseminating information in an expeditious manner that the center be headquartered in one central location but with regional treatment centers throughout the state. There was considerable discussion of the proposal received from the University of Arizona, Health Sciences Center.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATION SUPPORT THE CONCEPT OF REGIONALIZATION OF POISON CONTROL INFORMATION.

SECTION ON MEDICINE AND RELIGION

Clincial Pastoral Education Program

James G. Lawson, M.D., reported that many hospitals are going to full-time resident chaplains who have to be certified. There is a clinical pastoral education program and currently approximately 2,000 chaplains have been certified through the nation. RECEIVED FOR INFORMATION ONLY.

SECTION ON HEALTH EDUCATION

Warren L. Niccum, M.D. reported on the Health, Education, and Prevention Committee sponsored by the American Red Cross. They are currently planning to sponsor a seminar to be presented this Fall on school health. ArMA may be asked to help sponsor such a program. RECEIVED FOR INFORMATION.

SECTION ON SAFETY

Charles W. Pullen, M.D., reported that ArMA has introduced and actively supports legislation which will mandate the use of child auto restraint systems for children under four years of age. RECEIVED FOR INFORMATION ONLY.

SECTION ON PUBLIC HEALTH

Vita-Stat Automated Blood Pressure Recorders

William J. Thomas, M.D. summarized reports received from the Department of Health Services which evaluated automated blood pressure recorders. The reports indicate that the accuracy of these machines is within acceptable limits, but the public should be made aware that these devices should only be used for screening and that self-diagnosis should not be attempted. A complete report by Susan Dandoy, M.D., Director, Department of Health Services, was received for information.

SECTION ON EMERGENCY CARE AND DISASTER MEDICINE

Criteria For Emergency Room Centers

Willard R. Van Nostrand, M.D. explained that there is a need of official standards for emergency room centers which are being developed. Some of these facilities advertise 24 hour services when in fact a physician is on call for a part of the 24 hours and not present at the facility. In these cases, the word "emergency" should be disallowed. This subject will be discussed in more depth at the next meeting.

Dr. Van Nostrand also advised that plans are being developed to present the symposium on "Management of Radiation Accidents." RECEIVED FOR INFORMATION ONLY.

MEDICAL ECONOMICS COMMITTEE

Meeting of the Medical Economics Committee of the Arizona Medical Association, Inc., held at 810 West Bethany Home Road, Phoenix, on Thursday, Janaury 18, 1979, convened at 7:30 p.m., Richard W. Switzer, M.D., Chairman, presiding.

REVIEW OF ASSOCIATION SPONSORED INSURANCE PROGRAMS

Russ Waters, Southern California Agency, National Casualty Company, presented a proposal for updating the Association sponsored insurance programs. The objectives of the proposed insurance program are to centralize administration of all programs and to centralize local marketing operations. Centralized administration functions would mean the member would receive one statement each quarter to cover the various policies. Centralized marketing techniques would allow for more efficiency and economy with regard to mailings, advertising, etc. Claims would be handled more efficiently as there would be one phone number to call for the various policies. The policies offered in the program are High Limit A D & D, Life, Professional Overhead Expense, and Medical Insurance. The specifics of these policies were discussed at length.

It was determined to have Mr. Waters review the new requirements of professional corporations, being certain that Association insurance offerings would satisfy the new requirements and to circulate to the committee membership for approval of the program as presented.

FUTURE ASSSOCIATION ACTIVITIES WITH ICA

Daniel J. McAuliffe, Attorney from the firm of Snell & Wilmer informed the committee that his office has been contacted by the Attorney General with regard to their filing an anti-trust suit against the Arizona Medical Association of allegedly attempting to negotiate with the Industrial Commission for the purpose of setting fee schedules. The Attorney General has proposed that ArMA agree to a consent judgment. It was noted that ArMA has never negotiated with the Industrial Commission. Our only activity has been to make a presentation to the Commission as an aid to them when they set the schedules. There was considerable discussion relative to what action the Arizona Medical Association should take regarding the proposed suit.

Motion was made to recommend to the Boa of Directors that the Association not agree t the consent judgment proposed by th Attorney General. Motion died for lack second.

ICA FEE SCHEDULES

Although the prepared agenda identified review of the ICA Fee Schedules was in orde for the Committee during this meeting, th Chairman announced the subject is moot du to the Attorney General's proposed complair and the Committee's non-action. There was n discussion on this matter.

EXECUTIVE COMMITTEE

Meeting of the Executive Committee of th Arizona Medical Association, Inc. held at 8 West Bethany Home Rd., Phoenix, AZ Friday, January 19, 1979 a quorum bei present, convened at 6:46 p.m., Richard Dexter, M.D., President and Chairma presiding.

ARIZONA DEPARTMENT OF CORRECTIONS

Dr. Ian Louden, the new Medical Director the Arizona Department of Correction addressed the committee relative to the ne programs he was attempting to establish wi regard to health care for the inmates of th state correctional institutions, the additions had made to staff in an effort to improve a expand the role of the department, and th tremendous gratitude he felt for th overwhelming support and cooperation whi he had received from the Association, its sta and its individual membership since assumi his new post.

STATE OF ARIZONA PROPOSED ANTITRUST ACTION

Dan McAuliffe briefly reviewed for th committee the antitrust complaint proposed be filed shortly by the Attorney Gener against the Association, advising th committee that the only apparent alternati at this point to such filing was the entry of consent decree executed by the Associatio Mr. Jacobson advised the members regarding few exclussions which might be bargained f in the event it was determined that th Association did, in fact, wish to have a conse decree entered. Following a lengthy discussio it was

MOVED AND CARRIED TO RECOMMEND TO THE BOARD C DIRECTORS THAT THE ASSOCIATIO NOT ACCEPT THE CONSENT DECRE OFFERED BY THE STATE ATTORNE GENERAL RELATING TO A PROPOSE ANTITRUST ACTION AGAINST TH ASSOCIATION.

ANTITRUST GUIDE FOR ASSOCIATION MEMBERS

The committee briefly discussed th Antitrust Guide for Association Membe prepared by the American Society Association Executives previously forward to them for review. Mr. McAuliffe and M Jacobson both addressed the committe stating that, while the contents of th particular guide were good, it was somewh broader than what was required f Association purposes.

OVED AND CARRIED THAT LEGAL UNSEL, EDWARD JACOBSON AND AN MC AULIFFE, AND BRUCE BINSON WORK TOGETHER TO EPARE FOR ArMA MEMBERS A SET OF NTITRUST GUIDELINES MORE ECIFICALLY TAILORED FOR THE SOCIATION.

BOMEX VACANCIES

ecommendations to the Board of Directors ntained in January 16, 1979 letter of the ard of Medical Examiners — RECEIVED.

NATIONAL MEDICAL CARE SURVEY

he committee reviewed the letter of search Triagnle Institute dated January 10, 79 requesting intercession by the sociation on its behalf relative to a survey ing conducted in Yavapai County. It was the nsensus of opinion that response be made, vising Research Triangle Institute that rticipation in such survey was an individual oice and that the Association exercised no ntrol in such matters of physicians in the te.

LEGISLATIVE COMMITTEE

eeting of the Legislative Committee of the izona Medical Association, Inc. held at the ef Eaters Restaurant, 300 W. Camelback ad, Phoenix, on Saturday, January 27, 1979, nvened at 2:32 p.m., Selma E. Targovnik, D., Chairperson, presiding.

DEFINITION OF TERMS

CTIVE SUPPORT:

eans approval of bill and maximum staff time d financial expenditure (including legal unsel) will be made to achieve enactment.

ENERAL SUPPORT:

eans approval of the principle of the bill, but at staff time and financial expenditures will limited.

ACTION:

eans no position has been taken one way or other on the bill.

ON-SUPPORT:

eans disapproval of the bill, but that staff ne and financial expenditures will be limited defeat the bill.

CTIVE NON-SUPPORT:

eans disapproval of the bill and that aximum staff time and financial expenditure cluding legal counsel) will be expended to hieve defeat of the bill.

CTIVE STUDY:

eans the bill contains both supportable and posable elements.

LEGISLATIVE REVIEW

lternative to Medicaid

epresentative Diane McCarthy informed e Committee of an alternative to Medicaid r the State of Arizona. A program is rrently being developed with would provide r medical care for children only under the SDT portion of Title IXX. Much planning mains to be done on the plan, however, it is ticipated that legislation will be introduced r the program during the current session. here was considerable discussion, however, action taken at this time.

B. 2092 - Nurse Practitioner

he nurse practitioner legislation, H.B. 2092 as reviewed by the Committee. This bill ould place nurse practitioners under the ate Board of Nursing to establish the areas and rules of practice with minor collaboration with medicine. It would authorize the nurse practitioner to "prescribe" and do "minor surgery."

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT H.B. 2092.

Chiropractic - Removal of Limitations

The Committee received copy of the proposed legislative amendment to A.R.S. 32-925, Practice of Chiropractics, Limitations. The purpose of the proposed legislation is to remove some of the limitations currently on the practice of chiropractic and allow adjustment to adjacent tissues and contiguous structures of the spine.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT LEGISLATION REMOVING LIMITATIONS UPON THE PRACTICE OF CHIROPRACTIC.

S.B. 1044 - Chiropractic Continuing Education Requirements

S.B. 1044 has been introduced and will, if passed, remove the continuing education requirements for licensed chiropractors.

IT WAS MOVED AND CARRIED TO RECEIVE S.B. 1044 FOR INFORMATION ONLY.

Naturopathic

The Committee reviewed proposed legislation concerning naturopathic physicians which would increase their education requirements and require training in health care subjects. It was noted that the terms "non-surgical" and "drugless" were omitted in sections of the proposal.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT THE PROPOSED NATUROPATHIC LEGISLATION IF IT IS INTRODUCED.

H.B. 2067 - Osteopathic Advertising

The Committee reviewed H.B.2067 which, if passed, will allow advertising by osteopathic physicians along the lines of the Supreme Court decision on advertising. It will also allow their Board to hold informal hearings on cases of unprofessional conduct.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT H.B. 2067.

H.B. 2091 - Optometry

The Committee reviewed H.B. 2091 which proposes changes in the membership of the Board of Optometry and in continuing education requirements for optometrists.

IT WAS MOVED AND CARRIED TO RECEIVE H.B. 2091 FOR INFORMATION ONLY.

Radiologic Technologists ACT

The Attorney General's opinion relative to the Radiologic Technologists Act is that professional and practical nurses are required to obtain certification under the Radiologic Technologists Act prior to applying x-radiation to human beings under the supervision of a physician. This opinion appears to be in conflict with the Medical Practice Act. There was discusssion.

IT WAS MOVED AND CARRIED TO REFER THE ATTORNEY GENERAL'S OPINION RELATIVE TO THE RADIOLOGIC TECHNOLOGISTS ACT TO THE BOARD OF MEDICAL EXAMINERS AND REQUEST THAT THEY SEEK A RECONSIDERATION OF THE ATTORNEY'S OPINION.

H.B. 2060 - Certificate of Need

The Certificate of Need statute, if H.B. 2060 is passed, will be amended to eliminate all health care institutions except general hospitals from certificate of need requirements.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT H.B. 2060

H.B. 2061 - Blue Shield Payments to Assignees

The passage of H.B. 2061 would allow Blue Shield patients to assign to nonparticipating Blue Shield doctors their insurance payments. There is a significant percentage of physicians in Arizona who are not participating Blue Shield physicians. Blue Shield is the only company which would be affected by this legislation.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT H.B. 2061

H.B. 2033 - Public Funds for Abortions

Representative Diane McCarthy informed the Committee that H.B. 2033, which would prohibit the use of public funds for abortions except when necessary to save the life of the woman having the abortion, was introduced in the House. The bill was amended to expand the exceptions to include cases where there is a serious impairment of the woman's health, and in cases of rape and incest. Because of the amendments to H.B. 2033, the sponsor asked that the bill be removed. Mrs. McCarthy noted that the contents of H.B. 2033 are likely to show up as part of other health legislation during this session.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT LEGISLATION WHICH PROHIBITS THE USE OF PUBLIC FUNDS FOR ABORTIONS.

S.B. 1006 - Aflatoxin

The Committee reviewed S.B. 1006 which prohibits the manufacture, distribution, sale or use of aflatoxin contaminated feed. The bill defines "aflatoxin contaminated feed" as commercial feed which contains aflatoxin in any amount.

IT WAS MOVED AND CARRIED TO GENERALLY NON-SUPPORT S.B. 1006

H.B. 2036 - Pesticides

H.B. 2036 provides for the state chemist and the Director of the Department of Health Services to become members of the Board of Pesticide Control. It provides further that the Board shall adopt and enforce rules and regulations relating to application of pesticides in and around residential areas. Representative Diane McCarthy informed the Committee that the Governor's office is drafting legislation for introduction which would give more power, in this area, to the Department of Health Services.

IT WAS MOVED AND CARRIED TO ACTIVELY STUDY H.B. 2036 AND OTHER LEGISLATION WHICH MAY RELATE TO THE REGULATION OF APPLICATION OF PESTICIDES.

Podiatrist On Hospital Staffs

The Arizona Podiatry Association has drafted legislation for introduciton during this legislative session which would, if passed, mandate hospitals to allow for podiatrists on their staff. There was considerable discussion.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATON ACTIVELY OPPOSE LEGISLATIVE MANDATES OF THE COMPOSTION OF HOSPITAL MEDICAL STAFFS.

IT WAS MOVED AND CARRIED TO ACTIVELY STUDY LEGISLATION PROPOSED BY THE ARIZONA PODIATRY ASSOCIATION WHICH WOULD MAN-

DATE HOSPITALS TO ALLOW FOR PODIATRISTS ON THEIR STAFFS.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THEY REAFFIRM ArMA's APPROVAL OF THE JOINT POSITION STATEMENT ADOPTED DURING MEETING HELD NOVEMBER 29, 1976, BETWEEN REPRESENTATIAVES OF THE ARIZONA PODIATRY ASSOCIATION, CENTRAL ARIZONA ORTHOPEDIC SOCIETY AND THE ARIZONA HOSPITAL ASSOCIATION CONCERNING PODIATRY MEMBERSHIP TO HOSPITAL AFFILIATE STAFFS.

FINANCE COMMITTEE

The meeting of the Finance Committee of the Arizona Medical Association, held at 810 W. Bethany Home Rd., Phoenix, AZ, on Saturday, January 27, 1979, convened at 9:05 a.m., Neopito L. Robles, M.D., Treasurer and Chairman, presiding.

1980 BUDGET

Membership in outside Organizations

While discussing Account 504, "Dues, subscriptions & Contributions", specifically the "dues" portion, concern was expressed over the value of being members of the Arizona Council of Professions, Arizona Chamber of Commerce, etc. It was determined to drop our membership in the American Arbitration Association at the annual renewal date.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT, AT LEAST EVERY TWO YEARS, REPRESENTATIVES OF THE ORGANIZATIONS WHERE WE HOLD MEMBERSHIPS AND PAY DUES BE INVITED TO ATTEND A FINANCE COMMITTEE MEETING FOR THE PRUPOSE OF JUSTIFYING ArMA'S CONTINUED MEMBERSHIP.

Reports on Meetings Attended

During the discussion of accounts relating to having people attend meetings at ArMA's expense, the following action was taken:

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THEY REQUIRE THAT ANY PERSON ATTENDING MEETINGS AT ArMA'S EXPENSE SUBMIT A REPORT ON SAID MEETING WHICH WILL BE RECEIVED, REVIEWED AND EDITED FOR POSSIBLE PUBLICAITON IN ARIZONA MEDICINE AND MEDICAL MEMOS. REPORTS ON ANNUAL INTERIM MEETINGS OF THE AMERICAN MEDICAL ASSOCIATION WILL BE THE RESPONSIBILITY OF THE SENIOR DELEGATES.

IT was decided that, in order for the AMA delegation expenses to have a greater visibility on the financial statements, a separate account be established to which all expenses of AMA meetings, including travel, would be charged.

Budget Approval

Each account of the 1980 budget was reviewed in great detail, consuming a gareat deal of time, resulting in the following action:

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THEY SUBMIT THE FOLLOWING BUDGET RESOLUTION TO THE HOUSE OF DELEGATES IN APRIL:

RESOLUTION

Introduced by: BOARD OF DIRECTORS

Subject: 1980 CALENDAR YEAR BUDGET OF INCOME AND EXPENSE

WHEREAS, It is customary for the House of Delegates to approved the Budget of Income and Expenditures for the next succeeding calendar year of the Arizona Medical Association, Inc.; therefore be it

RESOLVED, That the following Budget of Income and Expenditure for the calendar year 1980 be adopted:

	INCOME	EXPENDITURES	
General Dept.	$617,095.00	$618,100.00	$ (1,005.00)
Commt. Dept.	127,000.00	88,200.00	38,800.00
Annl. Mtg.	72,400.00	56,740.00	16,460.00
Publ's Dept.	78,170.00	77,982.00	188.00
TOTAL	$894,665.00	$841,022.00	$53,643.00

; and be it further

RESOLVED, That the Annual dues of the Arizona Medical Asociation, Inc. be $250 for Active members, with $230 going to General Department Budget and $20 going to the Publishing Department Budget; and be it further

RESOLOVED, That the Service member dues be $62.50, with $42.50 going to th General Department Budget and $20 going t the Publishing Department Budget; and be further

RESOLVED, That the Intern or Resider Active member dues be $25, with $5 going t the General Department Budget and $20 goin to the Publishing Department Budget.

OTHER BUSINESS

Board of Directors Actions

Mr. Robinson reported that the Board Directors adopted the Finance Committee recommendations regarding the funding of th Pima immunization program and the ne proposal for setting committee budgets - RECEIVED.

EXECUTIVE COMMITTEE

The meeting of the Executive Committee of the Arizona Medical Association, Inc. held at 810 West Bethany Home Road, Phoenix, AZ, on Friday, February 9, 1979, a quorum being present, convened at 6:54 p.m., Richard L. Dexter, M.D., President and Chairman, presiding.

DEPARTMENT OF HEALTH SERVICES

Activity Report

Dr. Dandoy reported to the committee on several items of interest relative to recent and ongoing activities of the Department of Health Services, including among other things, its stand on the chemical dumping in a North Phoenix area and the posting of restrictions which was being attempted; and the attempts being made at renewing Medicaid statutes and the resultant issues re: Governor's child health bill.

Dr. Dandoy discussed developments pertaining to the Crippled Children's program, stating that a request for supplemental appropriations for the current fiscal year had been submitted; that a $3 million dollar increase in the budget for the upcoming year has already been approved by the Governor; that there has been recent discussion and investigation regarding the possibilities of separating the management of the crippled Children's program from that of the Crippled Children's Hospital; and that consideration is being given to strengthening the maternity portion of the program. Dr. Dandoy also reported on recent discussions with the Maricopa County Pediatirc Society relative to the need for a pediatric hospital in Phoenix.

Request for Support of Diabetes Control Demonstration Project

After a review and discussion of the reque of the Department of Health Services date January 31, 1979,

IT WAS MOVED AND CARRIED T SUPPORT THE ESTABLISHMENT OF DIABETES CONTROL DEMONSTRATIO PROJECT IN THE STATE OF ARIZONA.

CANCER NEWSLETTERS

The subject of the mailing of Cance Newsletters provided by the University Arizona for inclusion in our distribution Medical Memos was discussed by th committee and it was determined that th benefit received from the content of suc newsletters outweighed whatever minim charge might be required by way of addition postage.

IT WAS MOVED AND CARRIED T CONTINUE TO DISTRIBUTE TH CANCER NEWSLETTERS PROVIDED T THE ASSOCIATION BY THE UNIVERSIT OF ARIZONA.

INTERNAL REVENUE SERVICE AUDIT

Mr. Robinson presented the committee with brief update regarding the audit bein conducted by the IRS, advising that only on issue, that of "Unrelated Income," remaine that an appeal had been filed; and that th hearing, when held, would be held in Phoeni

MICA'S COMMITTEE TO REVIEW ARMA'S UNDERWRITING AND CLAIM REVIEW COMMITTEES

Mr. Robinson reported that MICA ha determined to review ArMA's Underwritin and Claim Review Committees. Mr. Robinso advised the committee that he would kee them informed of MICA's activities in th regard.

REVIEW OF BOARD OF DIRECTORS' AGENDA FOR 2/10/79

he agenda was discussed, with several ditions and changes being made.

CORRESPONDENCE

etter dated January 22, 1979, from Ian uden, M.D. — RECEIVED.

OTHER BUSINESS

quest for Funding - Arizona Chapter of ISA

he request of the Arizona Chapter of AMSA ted February 7, 1979 for $300.00 to aid in ding 15 representatives to Denver in March r the AMSA National Convention was viewed by the committee.

T WAS MOVED AND CARRIED THAT NDING IN THE AMOUNT OF $300.00 THE ARIZONA CHAPTER OF AMSA BE PROVED.

ouse Bill 2402

Ir Barnett presented to the committee a aft of House Bill 2402 intended for mediate introduction in the legislature, hich was aimed at recognizing the undation and exempting it from antitrust igation. Because of the time element volved, it was the consensus of opinion that e same be presented to the Board of irectors at its upcoming meeting requesting pport of the concept of House Bill 2402.

T WAS MOVED AND CARRIED TO ECOMMEND TO THE BOARD OF IRECTORS THAT THE ASSOCIATION JPPORT THE CONCEPT CONTAINED IN HE DRAFT OF HOUSE BILL 2402, JBJECT TO REVIEW BY ANTITRUST OUNSEL.

AD HOC MEMBERSHIP COMMITTEE

he meeting of the Ad Hoc Membership mmittee of the Arizona Medical sociation, Inc. held at 810 West Bethany me Road, Phoenix, Arizona, on Saturday, bruary 10, 1979, convened at 1:22 p.m., chard L. Dexter, M.D., President and airman, presiding.

DISTRICT DIRECTORS' REPORT

everal of the district directors reported to e committee regarding the number and types groups which constitute non-members in eir specific areas, including new physicians, MO physicians and hospital staff physicians.

REASONS FOR LACK OF INTEREST AND NON-PRTICIPATION

The committee discussed the lack of personal ntact with the groups involved and the fact at many physicians do not feel the AMA is ing anything for them as being the two ajor reasons for non-participation in ArMA. was agreed that a concentrated effort would made by all district directors to appear fore and speak to HMOs and governmental oups, hospital medical staffs and other ysician-oriented gatherings in an effort to esent the advantages of membership in the ssociation.

As an added incentive, because of the pending wsuit by the Association against the State ttorney General and the fact that the sociation was now taking a stand on behalf of s member physicians, it was determined that e forthcoming Medical Memos reporting on uch lawsuit be sent to *all licensed physicians* in the tate as an indication of what the Association an do.

SUGGESTIONS

Texas Medical Association

Sample solicitation letter used by the Texas Medical Association — RECEIVED.

AMA's Department of Membership Development

Bruce Robinson reported that the AMA's Department of Membership Development was beginning to gear up for a special membership project in which it would designate 10-15 states to participate and that indication had been made that Arizona, if interested, could be one of those. the project would involve AMA personnel setting up seminars within the state in an effort to project new ideas or rework old ones for membership solicitation. It was the consensus of opinion that Mr. Robinson contact the Department of Membership Development at the AMA to advise the Arizona's interest in participating in the project and attempt to begin scheduling seminars/workshops, etc. as soon as possible.

BOARD OF DIRECTORS

The meeting of the Board of Directors of the Arizona Medical Association, Inc. held at 810 W. Bethany Home Road, Phoenix, Arizona on Saturday, February 10, 1979, a quorum being present, convened at 10:08 a.m., Richard L. Dexter, M.D., President and Chairman, presiding.

MOUNTAIN STATES LEGAL FOUNDATION

James G. Watt, President and Legal Officer of the Mountain States Legal Foundation, addressed the Board regarding the Foundation, its pruposes, present activities and future aims and goals as it relates to legal representation on enconmic issues of individulas and groups in an eight-state area.

ARMPAC

Appointment of new chairman — NO ACTION

BOARD OF DIRECTORS

Central District Director Vacancy

IT WAS MOVED AND CARRIED TO APPOINT RUDOLF KIRSCHNER, M.D. TO COMPLETE THE TERM OF JAMES A . AUSTIN, M.D. AS CENTRAL DISTRICT DIRECTOR.

Southeastern District Director Vacancy

IT WAS MOVED AND CARRIED TO APPOINT KENNETH A. DREGSETH, M.D. TO COMPLETE THE TERM OF EDWARD R. CURTIS, M.D. AS SOUTHEASTERN DISTRICT DIRECTOR.

BOMEX Appointments

Discussion was held regarding the vacancies which would be created in 1979 on the Board of Medical examiners and the normal practice of the Association to recommend physicians to fill such vacancies to the Governor of the State of Arizona.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE GOVERNOR OF THE STATE OF ARIZONA FOR CONSIDERATION AS MEMBERS OF THE BOARD OF MEDICAL EXAMINERS JAMES E. BRADY, JR., M.D., RICHARD L. DEXTER, M.D., JOHN J. STANDIFER, M.D. AND MANUS R. SPANIER, M.D., THE LATTER RECOMMENDATION BEING CONTINGENT UPON DR. SPANIER INDICATING A DESIRE TO AGAIN SERVE ON SUCH BOARD.

A. H. Robins "Community Service Award"

IT WAS MOVED AND CARRIED THAT THE A. H. ROBINS "COMMUNITY SERVICE AWARD" BE PRESENTED AT THE 1979 ANNUAL MEETING OF THE ASSOCIATION TO MERLIN K. DuVAL, M.D.

Following a discussion by the membership of the problems encountered in timely selecting a candidate for Receiving the A. H. Robins "Community Service Award" each year,

IT WAS MOVED AND CARRIED THAT AN AD HOC COMMITTEE BE ESTABLISHED TO PRESENT TO THE BOARD NOMINATIONS FOR THE A. H. ROBINS "COMMUNITY SERVICE AWARD" TO BE PRESENTED IN 1980.

EXECUTIVE COMMITTEE

Membership Classification Changes

Maricopa County Medical Society

Hayes Caldwell, M.D. - Acitve to Associate - Account Retirement - Dues Exempt - Effective 5/1/79.

2. Louis P. Lutfy, M.D. - Active to Active Over 70 -Account Age - Dues Exempt - Effective 1/1/79.

3. 3George A. Spendlove, M.D. - Active to Associate -Account retirement - Dues Exempt - Effective 1/1/79.

Mohave County Medical Society

1. Margo C. Sobey, M.D. - Active to Associate -Account Retirement - Dues Exempt - Effective 1/1/79.

Pima County Medical Society

1. Jay H. Anderson, M.D - Active to Affiliate - Account Armed Forces - Dues exempt - Effective 1/1/79.

2. Carl Z. Berry, M.D. - Active to Associate - Account Retirement - Dues Exempt - Effective 1/1/79.

3. Michael A. Boxer, M.D. - Requests Dues Exemption Continued for 1979.

4. Gerriet A. Janssen, IV, M.D. - Active to Affiliate -Account Out of State - Dues Exempt - Effective 1/1/79.

5. Gerd T. Schloss, M.D. - Active to Associate -Account Retired - Dues Exempt - Effective 1/1/79.

6. Stanley S. Tanz, M.D. - Active to Associate -Account Retired - Dues Exempt - Effective 1/1/79.

Yuma County Medical Society

1. Abe I Podolsky, M.D. - Active to Active Over 70 - Account Age - Dues Exempt - Effective 1/1/79.

2. Matthew L. Wong, M.D. - Active to Active Over 70 -Account Age - Dues Exempt - Effective 1/1/79.

Memberships Approved

Student Members:

1. Ronald D. Hanson
2. William B. Ethridge

AD HOC COMMITTEE ON AN ECONOMIC ORGANIZATION FOR ARIZONA PHYSICIANS

Legal Counsel Comment

Letter dated February 9, 1979 from Frederick K. Steiner, Jr., Esq — RECEIVED.

Committee's Recommendation

The action of the Ad Hoc Committee on an Economic Organization for Arizona Physicians taken at its January 6, 1979 meeting was received by the Board — NO ACTION.

FINANCE COMMITTEE

The recommendations of the Finance Committee made subsequent to its January 27, 1979 meeting were considered by the Board and the following action taken.

Membership Justification

IT WAS MOVED AND CARRIED THAT, AT LEAST EVERY TWO YEARS, REPRESENTATIVES OF THE ORGANIZATIONS WHERE THE ASSOCIATION HOLDS MEMBERSHIPS AND PAYS DUES BE INVITED TO ATTEND A FINANCE COMMITTEE MEETING FOR THE PURPOSE OF JUSTIFYING ArMA'S CONTINUED MEMBERSHIP.

Reports from Meeting Attendees

IT WAS MOVED AN CARRIED THAT THE ASSOCIATION REQUIRE THAT ANY PERSON ATTENDING MEETINGS AT ARMA' EXPENSE SUBMIT A REPORT ON SAID MEETING WHICH WILL BE RECEIVED REVIEWED AND EDITED FOR POSSIBLE PUBLICATION IN ARIZONA MEDICINE AND MEDICAL MEMOS. REPORTS ON ANNUAL AND INTERIM MEETINGS OF THE AMERICAN MEDICAL ASSOCIATION WILL BE THE RESPONSIBILITY OF THE SENIOR DELEGATE.

1980 Budget Proposal

IT WAS MOVED AND CARRIED TO ADOPT AND PRESENT TO THE HOUSE OF DELEGATES AT THE 1979 ANNUAL MEETING THE BUDGET PREPARED BY THE FINANCE COMMITTEE FOR 1980, WITH THE CONTINGENCY BALANCE TO BE LISTED AS "ALLOCATION FOR FUTURE PROJECTS."

GOVERNMENTAL SERVICES COMMITTEE

The recommendations of the Governmental Services Committee made subsequent to its January 10, 1979 meeting were considered by the Board and the following action taken.

"A Discursive Dictionary of Health Care"

IT WAS MOVED AND CARRIED THAT THE ARIZONA MEDICAL ASSOCIATION RECOMMEND TO THE ARIZONA HSA'S AND OTHER GOVERNMENTAL AND QUASI-GOVERNMENTAL ORGANIZATIONS THAT THEY ADOPT THE DICTIONARY "A DISCURSIVE DICTIONARY OF HEALTH CARE" AND FURTHER, RECOMMEND TO THE AMERICAN MEDICAL ASSOCIATION THAT THIS DICTIONARY BE MADE THE REFERENCE DOCUMENT FOR P.L. 93-631.

National Health Insurance

IT WAS MOVED AND CARRIED THAT THE FOLLOWING RESOLUTION BE INTRODUCED TO THE ARIZONA MEDICAL ASSOCIATION'S HOUSE OF DELEGATES 1979 ANNUAL MEETING:

"WHEREAS, It is a recognized fact that Americans have the best medical care system in the world today, and most polls indicate the public is generally satisfied with both the quality and quantity of medical services; and

WHEREAS, The polls have consistently reflected that the American people hold their individual physician in higher regard and trust than any other professional; and

WHEREAS, It is this very personal doctor-patient relationship that will be dismantled and ultimately destroyed by national health insurance if the freedom of the patient to choose his system of health care is not protected; and

WHEREAS, There is always an obligation to improve any system: therefore, be it

RESOLVED, That the Arizona Medical Association recommends to the Congress of the United States of America modifications to our present health care system embodying the following principles:

1. Requiring minimum standards of adequate benefits in all health insurance policies sold in the United States with appropriate deductible and co-insurance.
2. It is the responsibility of the state and/or local governments to provide medically for those individuals who are unfortunate enough (through no fault of their own, i.e., age, disability, financial hardship, etc.) not to be able to provide for their own medical care.
3. A nationwide program by the private insurance industry of America (and government if necessary for reinsurance) to make available catastrophic insurance coverage for those illnesses and individuals where the economic impact of a catastrophic illness could be tragic. All catastrophic coverage should have an appropriate deductible and co-insurance to make it economically feasible and to avoid abuse.
4. A program developed pursuant to these principles should be adminstered at the state level with national standardization through federal guidelines assuring the patients the right to choose their own system of medical care."

Definition of Provider and Consumer

IT WAS MOVED AND CARRIED TO REQUEST THE GOVERNMENTAL SERVICES COMMITTEE TO PREPARE, IN RESOLUTION FORM FOR INTRODUCTION TO THE HOUSE OF DELEGATES AT THE 1979 ANNUAL MEETING OF THE ASSOCIATION, A RECOMMENDATION BY ARMA RELATIVE TO AMENDING P.L. 93-631, SEC. 1531 (3) (B) (1) DURING THE 96TH CONGRESS.

LEGISLATIVE COMMITTEE

Confirmation of Appointment

IT WAS MOVED AND CARRIED THAT THE APPOINTMENT OF RICHARD O. FLYNN, M.D., AS A MEMBER OF THE LEGISLATIVE COMMITTEE BE CONFIRMED.

Legislative Mandates for Hospital Medical Staffs

The recommendation of the Legislative Committee made subsequent to its January 27, 1979 meeting were considered by the Board and the following action taken.

IT WAS MOVED AND CARRIED THAT THE ARIZONA MEDICAL ASSOCIATION ACTIVELY OPPOSE LEGISLATIVE MANDATES OF THE COMPOSITION OF HOSPITAL MEDICAL STAFFS.

IT WAS MOVED AND CARRIED THAT THE ARIZONA MEDICAL ASSOCIATION REAFFIRM ITS APPROVAL OF THE JOINT POSITION STATEMENT ADOPTED DURING MEETING HELD NOVEMBER 29, 1976, BETWEEN REPRESENTATIVES OF THE ARIZONA PODIATRY ASSOCIATION, CENTRAL ARIZONA ORTHOPEDIC SOCIETY, AND THE ARIZONA HOSPITAL ASSOCIATON CONCERNING PODIATRY MEMBERSHIP TO HOSPITAL AFFILIATE STAFFS.

House Bill 2402

IT WAS MOVED AND CARRIED THAT THE ARIZONA MEDICAL ASSOCIATION ACTIVELY SUPPORT HOUSE 2402 PROVIDING FOR PHYSICIANS' INSURANCE ADMINISTRATOR ASSOCIATIONS WHICH WILL EXEMPT THEIR ACTIVITIES FROM THE STATE ANTITRUST ACT.

AD HOC MALPRACTICE INSURANCE CRISIS COMMITTEE

Renewal of Section of H.B. 2001

The Board considered the recommendation of the Ad Hoc Malpractice Insurance Crisis Committee made subsequent to its January 17 1979 meeting and took the following action.

IT WAS MOVED AND CARRIED THAT THE ARIZONA MEDICAL ASSOCIATION ACTIVELY SUPPORT THE RENEWAL OF PROVISIONS IN H.B. 2001 UNDER SECTIONS 20-1722, 20-1723, AND 20-1724

PROFESSIONAL COMMITTEE

The Board considered the recommendations of the Professional Committee made subsequent to its January 16, 1979 meeting and took the following action.

Regionalization of Poison Contro Information

IT WAS MOVED AND CARRIED TO APPROVE THE CONCEPT OF AN UPGRADED ARIZONA POISON CONTROL AND DRUG INFORMATION CENTE AS PROPOSED BY THE UNIVERSITY OF ARIZONA HEALTH SCIENCES CENTER ON NOVEMER 24, 1978. FURTHER, IT WAS A DETERMINED TO REFER THI LEGISLATION PROVIDING FOR A FREE-STANDING POISON CONTROL INFORMATION CENTER TO THE LEGISLATIVE COMMITTEE FOR ITS CONSIDERATION

Health Insurance Policies and Second Opinions.

IT WAS MOVED AND CARRIED THAT THE ARIZONA MEDICAL ASSSOCIATION GO ON RECORD AS RECOMMENDING TO THE DEPARTMENT OF INSURANCE THAT HEALTH INSURANCE POLICIES WRITTEN WITHIN THE STATE OF ARIZONA ALLOW BENEFITS FOR SECOND OPINIONS AT THE REQUEST OF THE PATIENTS.

Physical Exams

The request of the Pima County Medica Society dated January 16, 1979 relative to report by its Committee for Public Helath School and Sports Medicine on pre participation sports physical examinations wa considered by the Board.

IT WAS MOVED AND CARRIED TO REFER THE REQUEST OF THE PIMA COUNTY MEDICAL SOCIETY, TOGETHER WITH ITS REPORT REGARDING PRE-PARTICIPATION SPORTS PHYSICAL EXAMINATIONS TO THE SECTION ON SPORTS MEDICINE OF THE PROFESSIONAL COMMITTEE FOR ITS CONSIDERATION AND ACTION WITH THE ARIZONA INTERSCHOLASTIC ASSOCIATION.

AMA DELEGATION

Ad Hoc Committee on the Principles of Medical Ethics

Request for Comments from the AMA dated January 15, 1979 — NO ACTION.

CORRESPONDENCE

Letter from student attendees at AMA Interim Meeting — RECEIVED.

Letter from Bruce Evans dated 1/15/79 – RECEIVED.

OTHER BUSINESS

Western Physicians Purchasing Association

Dr. Kahle briefly reported on the WPPA Board of Directors meeting held in Phoenix o ruary 3, 1979, advising that the catalogues e now available and discussing several of new items which had recently been added. eral of the members interjected their mendous satisfaction with the discounts service they had already received through new purchasing association.

posed Antitrust Action by the State of zona

WAS MOVED AND CARRIED THAT E ARIZONA MEDICAL ASSOCIATION T ACCEPT THE CONSENT DECREE FERED BY THE STATE ATTORNEY NERAL RELATING TO A PROPOSED TITRUST ACTION AGAINST THE SOCIATION.

ion for Declaratory Judgement Against the te Attorney General

WAS MOVED AND CARRIED THAT UNSEL FOR THE ARIZONA MEDICAL SOCIATION IMMEDIATELY FILE A MPLAINT AGAINST THE STATE TORNEY GENERAL SEEKING A LCARATORY JUDGMENT THAT IT IS E LEGAL RIGHT OF THE ASSOCIA-N, ON BEHALF OF ITS MEMBERS, TO PEAR BEFORE CERTAIN ENTITIES AND OVIDE INFORMATION OR TESTI-NY RELATING TO COMPENSATION VELS FOR PHYSICIANS' SERVICES AND AT SUCH PRACTICE IS NOT LATIVE OF ANY PROVISION OF THE IZONA ANTITRUST ACT.

MATERNAL & CHILD HEALTH CARE COMMITTE

The meeting of the Maternal & Child Health Care Committee of the Arizona Medical Association, Inc. held at 810 W. Bethany Home Road, Phoenix, Arizona on Saturday, February 24, 1979, convened at 12:25 p.m, William C. Scott, M.D., Chairman, presiding.

PLANNED PARENTHOOD PROPOSAL

Action of the Board of Directors taken 12/16/78 regarding Planned Parenthood proposal — RECEIVED.

HOME DELIVERIES BY LAY MIDWIVES

William J. Moore, M.D. Report

Dr. Moore briefly discussed his written memorandum to the Chairman dated January 29, 1979 and the ultimate conclusions of legal counsel regarding assimilation of data pertaining to non-hospital deliveries and complications resulting therefrom. Following a lengthy discussion of the matter, it was determined that a voluntary reporting system would be instigated through the hospitals, OB/GYN Society and others and that such information for the present would be fed to and assembled by the Department of Health Services. Additionally, Dr. Scott would, as Chairman of the committee, contact Dr. Dandoy, as Director of the Department of Health Services advising her that a voluntary reporting system was being attempted, but voicing the committee's concern and requesting that she consider a mandatory requirement for such reporting, allowing an advisory committee to oversee the procedure. The committee felt Dr. John Kelly would be an appropriate choice to head up such an advisory committee, should one ultimately be created.

Department of Health Services Correspondence

Letter dated 2/13/79 from the Department of Health Services re: lay midwifery program — RECEIVED.

At the request of the Chairman, Dr. Baum addressed the committee regarding the IPO grant referred to in the Department of Health Services February 13th letter, and advised that the grants which had previously been given to only states having a high infant mortality rate were now being designated for other states as well and that the grant funds would be designed to be used for 1) services in areas of the state having unfavorable mortality rates; 2) assistance in connection with the Arizona Perinatal Program; 3) augmentation of the Department of Health Services' capability to plan and conduct maternity programs outside the grant; and 4) emphasizing adolescent pregnancy and its related problems. At this point, Dr. Gabel also addressed the committee regarding the long-range planning of the Arizona Perinatal Program in this regard.

SECTION ON PERINATAL HEALTH

Report on Genetic Services

Report of William J.R. Daily, M.D. as Chairman of Subcommittee on Perinatal Health — RECEIVED.

Thomas R. Harris, M.D.'s Letter of 8/11/78 — RECEIVED.

Following a discussion of Dr. Harris' letter and report in conjunction with the report of Dr. Daily, it was determined that the chairman establish a subcommittee on genetic services and named Harold D. Gabel, M.D. to act as Chairman

ArMA's Annual Meeting

Harold D. Gabel, M.D.'s Letter of 12/21/78 — RECEIVED

Following discussion regarding the Scientific Assembly Committee meeting attended by Dr. Gabel as a representative of the OB/GYN Society, and past and present procedures for choosing guest speakers for the annual meetings of the Association.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE SCIENTIFIC ASSEMBLY COMMITTEE THAT IT STRONGLY CONSIDER SELECTING INDIVIDUAL SPEAKERS, WITHOUT LOOKING AT OR BEING RESTRICTED TO ANY SPECIFIC UNIVERSITY, WHEN CHOOSING GUEST FACULTY FOR THE 1981 AND SUBSEQUENT ANNUAL MEETINGS OF THE ASSOCIATION.

SECTION ON SERVICES FOR CHILDREN

Following a review and discussion of the Alternative for Providing a Comprehensive Children's Health Care Program in Arizona prepared by the Department of Economic Security on Janaury 31, 1979.

IT WAS MOVED AND CARRIED TO TABLE ANY EVALUATION, RECOMMENDATIONS OR CONSIDERATION RELATIVE TO THE DEPARTMENT OF ECONOMIC SECURITY'S JANUARY 31, 1979 ALTERNATIVE FOR PROVIDING A COMPREHENSIVE CHILDREN'S HEALTH CARE PROGRAM IN ARIZONA.

CORRESPONENCE

Appointment of William Carlile, M.D.

Ted Baum M.D.'s letter of 12/15/78 re: appointment of Dr. Carlile as Chief, Section of Maternal/Perinatal Health, Bureau of Maternal & Child Health, DHS — RECEIVED.

Duchenne Muscular Dystrophy

National Foudnation - March of Dimes letter dated 10/20/78 — RECEIVED.

OTHER BUSINESS

AMA Resolutions & Reports

Resolutions & Reports Relating to infants and Children forwarded by the AMA on 2/2/79 — RECEIVED.

House Bill 2336

Dr. Gabel advised the committee that House Bill 2336 relating to maternity insurance was schedueld to be heard in committee on Monday, February 26, 1979. After a lengthy discussion of the matter.

IT WAS MOVED AND CARRIED TO REQUEST GARY L. BARNETT, ON ON BEHALF OF THE ASSOCIATION, TO REQUEST A ONE WEEK CONTINUANCE OF THE HEARING SCHEDULED FOR FEBRUARY 26, 1979 ON HOUSE BILL 2336 TO ENABLE THE COMMITTEE TO ASSEMBLE A GROUP TO APPEAR AT SUCH HEARING AND PRESENT INFORMATION NECESSARY FOR PROPER EVALUATION OF SUCH PENDING LEGISLATION.

The following members were considered as possible attendees at the hearings referred to: Walter B. Cherny, M.D., Sister Alice Montgomery, Raymond J. Jennett, M.D., H. Belton Meyer, M.D.; and Dr. Gabel was designated to orally present the committee's request to Mr. Barnett with the foregoing suggested names.

Committee Makeup

Dr. Baum suggested that at the time of the annual meeting of the Association and appointment of committee members additional pediatricians be considered to more evenly balance the membership of the committee.

Future Medical Meetings

CONTINUING MEDICAL EDUCATION

The following institutions and organizations have been accredited for their continuing medical education programs by the Liaison Committee on Continuing Medical Education.

Arizona Heart Institute
Arizona Medical Association, Inc.
Arizona State Hospital, Phoenix
Desert Samaritan Hospital, Mesa
Good Samaritan Hospital, Phoenix
Health Maintenance Associates
Phoenix Indian Medical Center
Phoenix Psychiatric Council
Maricopa County General Hospital, Phoenix
Memorial Hospital, Phoenix
St. Luke's Hospital & Medical Center, Phoenix
St. Joseph's Hospital & Medical Center, Phoenix
Tucson Hospitals Medical Education Program, Tucson
U of A College of Medicine
Veterans Administration Center, Prescott
Veterans Administration Hospital, Phoenix

The accredited institutions and organizations above produce a variety of continuing medical education programs. Each accredited institution and organization is responsible for designating which of these programs meet ArMA's requirements for Category 1 credit. Physicians who participate in programs which are designated Category 1 by accredited institutions will receive Category 1 credit toward the ArMA Certificate in CME and the AMA's Physician's Recognition Award.

APRIL

88th Annual Meeting: Arizona Medical Association
April 25—29, 1979. Sponsor: Arizona Medical Association, Inc. Contact: Bruce E. Robinson, Executive Director, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Approved for category 1 credit.

Health Hazard Appraisal: Clinical Information for Consumer and Ptractitioners
April 21 & 22, 1979. Sheraton-Place Hotel, San Francisco,CA. Sponsor: University of California, San Francisco. Contact Ms. Bruce, Univ. of California, San Francisco, Continuing Education Health Sciences, 1343 Third Ave., San Francisco, CA 94143.

MAY

Update: Primary Care 1979
May 2-5, 1979, Univ. of Arizona, Arizona Health Sciences Center, 1501 N. Campbell Ave., Tucson, AZ Sponsor: Univ. of Arizona College of Medicine, Office of CME. Cntact: Faith Carlisi, Conference Coordinator, Office of CME, Arizona Health Sciences Center, Tucson, AZ 85724. Approved for 30 hours of Category 1 credit.

Advanced Cardiac Life Support Program Recertification Program
May 18, 1979. Arizona Medical Association offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner, ArMA Offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Approved for 16 hours of category 1 credit.

NEUROSURGICAL PROBLEMS COURSE:
May 19, 1979. University of Arizona Health Sciences Center, Tucson, AZ. Sponsor: Office of CME, UAHSC. Contact: Office of Continuing Medical Education, Univ. of Arizona Health Sciences Center, Tucson, AZ 85724 Attn: Faith Carlisi. Approved for 8 hours of category 1 credit.

JUNE

Current Concepts in Obstetrics & Gynecology and their Clinical Applications
June 14-16, 1979. Santa Fe Hilton Inn, Santa Fe, N. M. 87501. Sponsor: Symposia de Santa Fe & New Mexico Medical Society. Contact: Walter J. Levy, M.D. P.O. Box 5175, Santa Fe, N.M. 87502. Approved for 16 ½ hours of prescribed CME credit.

MONTHLY OR WEEKLY

Shrine Medics Meeting
Second Tuesday of each month, Doctors Hospital, 5:45 p.m. J. South Classroom. Sponsor: Shrine Medics. Contact: Robert C. Briggs, M.D., 5121 N. Central Ave., Phoenix, AZ 85012.

Office Psychiatry for the Primary Provider
2nd Monday of month, 4811 N. 7th Street, Phoenix, AZ. Sponsor: Arizona Health Plan. Contact: T.R. Bittker, M.D., Box 5000, Phoenix, AZ 85010. Approved for category 1 credit.

Counter Transference Group
Weekly, Thurs. 8—10 p.m. Sponsor: Phoenix Psychiatric Council. Contact: James E. Campbell, M.D., 5051 N. 34th St., Phoenix, AZ 85018. Approved for 2 hours category 1 credit.

Monthly Meeting of Tucson Radiologists
Last Tues. of month. Plaza International, Tucson, AZ. Sponsor: U of A Medical Center, Dept. of Radiology. Contact: Irwin M. Freundlich, M.D., U of A Health Sciences Center, Dept. of, Radiology, Tucson, AZ 85724. Approved for 2 hours category 1 credit.

Pediatric Grand Rounds
Tuesday 7:30-8:30 a.m in Phoenix: 1st Tues.—Phoenix Indian Hospital, 2nd Tues.—Maricopa County Hospital, 3rd Tues.—Good Samaritan Hospital, 4th Tues.—St. Joseph's Hospital. Sponsor: Maricopa County Hospital (Phoenix Hospital's Affiliated Pediatric Program). Contact: J. Kipp Charlton, M.D., 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

Review of Forensic Pathology Current Case, Special Topics
Thursday, weekly, 11 a.m., 120 S. 6th Ave., Phoenix, AZ. Sponsor: Arizona Society of Pathologists. Contact: H.H. Karnitschnig, M.D., 120 S. 6th Ave., Phoenix, AZ. Approved for 1 hour per session category 1 credit.

Staff Education Conference
Wednesdays, weekly, 1 p.m., Arizona State Hospital, Phoenix, AZ. Sponsor: Arizona State Hospital. Contact: Howard E. Wulsin M.D., Arizona State Hospital, 2500 E. Van Buren, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

BARROW NEUROLOGICAL INSTITUTE

Medical Education
Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Sponsor: St Joseph's Hospital & Medical Center. Contact: John R Green, M.D. Approved for 1 hour category 1 credit.

Neurology Teaching Conference
Tuesdays, 8:30-9:30 a.m., Eighth Floor Conf. Room.

Neurosurgery Morbidity Conference
Wednesdays, 8:15-9:15 a.m., on first and third weeks, Eighth Floor Conference Room.

Neuro-ophthalmology Conference
Tuesdays, 7:30 a.m. in 8th floor neurology conference room.

Spinal Injury Conference
Wednesdays, 8:15-9:15 a.m., on second and fourth weeks, in Neuropathology Conf. Rm.—a multidisciplinary review of admission by neurosurgeons, orthopedists, and rehabilitation specialists

Neuropathology of Gross Specimens Conference
Thursday, 7:30-8:30 a.m. in the Morgue.

Neurology-Neurosurgical Clinical-Neuroradiological and Neuropathological Conference
Fridays, 8-9 a.m., First Floor Conference Rm.

Neuropathology or Neuroradiology Conferences
Friday, 9 a.m., Neuropathology in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

Neurorehabilitation Conference
Tuesdays, noon, 8th Floor Conference Rm.

Neurosurgical Journal Club
Saturdays, 9-11 a.m. in Eighth Floor Conference Rm.

ogy in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

CAMELBACK HOSPITAL

5055 N. 34th St., Phoenix, AZ 85018. Sponsor: Camelback Hospital. Contact: Medical Director.

Patient Staffing Conference
Three times weekly.

CARDIOVASCULAR NUCLEAR MEDICINE UPDATE:

INDICATIONS & TECHNIQUES

PRESENTED BY
ARIZONA HEART INSTITUTE
and
SCRIPPS CLINIC & RESEARCH FOUNDATIONS

Saturday, May 12, 1979
Marriott's Camelback Inn
Scottsdale, Arizona

PURPOSE

Radioisotopic studies are one of the fastest growing areas of cardiovascular medicine, providing an accurate and important form of noninvasive diagnosis. The latest techniques used in myocardial perfusion imaging, gated wall motion studies, and pyrophosphate acute myocardial infarct imaging will be presented by a distinguished faculty of leading nuclear medicine specialists. Among the topics addressed in this one-day seminar will be: indications for scanning in asymptomatic patients, comparisons of individual stress ECG tests with stress tests combined with nuclear scanning, correlation of scintigraphy with coronary arteriography, and the role of nuclear medicine in the evaluation of postsurgical patients.

This program, directed toward the practical application of nuclear diagnosis in cardiovascular medicine, will be of benefit to cardiologists, internists, family physicians, radiologists, nuclear medicine specialists, and other specialty groups interested in a state-of-the-art discussion of nuclear diagnostics in cardiovascular medicine.

ACCREDITATION

This continuing medical education activity meets the criteria for 6 credit hours in Category I of the Physician's Recognition Award of the American Medical Association, and is acceptable for 6 Elective hours by the American Academy of Family Physicians.

REGISTRATION

Registration Fee $100
Residents, Technicians, and Nurses $50
Registration Fee includes lunch

8:30	**Which Noninvasive Test and When? Applying Serial Bayesian Analysis**	Daniel S. Berman, M.D.
	Stress Radionuclide Ventriculography to Detect Coronary Artery Disease	William L. Ashburn, M.D.
9:50	**BREAK**	
10:20	**Hot Spot Myocardial Infarct Imaging**	James T. Willerson, M.D.
	Practical Application of Thallium-201 Scintigraphy in the Coronary Care Unit	Frans J. Th. Wackers, M.D.
11:45	**LUNCH**	
1:15	**Assessing Acute Myocardial Infarction by Equilibrium Blood Pool Scintigraphy**	Daniel S. Berman, M.D.
	Sizing Acute Myocardial Infarcts Scintigraphically	James T. Willerson, M.D.
2:35	**BREAK**	
3:05	**Pitfalls in Reading Thallium-201 Images**	Frans J. Th. Wackers, M.D.
	"First Pass" & "Equilibrium" Radionuclide Angiography— Methods & Applications	William L. Ashburn, M.D.
4:25	**What Can You and Your Patients Expect From Nuclear Cardiology**	Panel: Drs. Ashburn, Berman, Wackers, & Willerson

FACULTY

William L. Ashburn, M.D.
Division of Nuclear Medicine
University of California, San Diego
San Diego, CA

Daniel S. Berman, M.D.
Department of Nuclear Medicine
Cedars-Sinai Medical Center
Los Angeles, CA

Frans J. Th. Wackers, M.D.
Section of Cardiology
Yale University School of Medicine
New Haven, CT

James T. Willerson, M.D.
Division of Cardiology
University of Texas Health Science Center
Dallas, TX

DESERT SAMARITAN HOSPITAL

Wednesday evenings, 7 p.m. Sponsor: Desert Samaritan Hospital. Contact: L. A. Rosati, M.D., Laboratory, Desert Samaritan Hospital, Mesa, AZ 85202. Approved for category 1 credit.

GOOD SAMARITAN HOSPITAL

Clinical Cancer Conference
3rd Wednesday, every month, Butler Bldg. Conference Rm. Good Samaritan Hospital. Contact: John A. Bruner, M.D., 926 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour per session category 1 credit.

Pulmonary Disease Grand Rounds
Mondays, 12 Noon, D-5 North Conf. Rm., Good Samaritan Hospital, Phoenix, AZ. Sponsor: Pulmonary Disease Teaching Service, Good Samaritan Hospital. Contact: Bernard E. Levine, M.D., Pulmonary Function Laboratory, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour category 1 credit.

MARYVALE SAMARITAN HOSPITAL

Continuing Medical Education Program
Maryvale Samaritan Hospital, every other Wednesday, 7-8 a.m., January 25, 1978

MARICOPA COUNTY GENERAL HOSPITAL

2601 E. Roosevelt, Phoenix, AZ 85008. Sponsor: Maricopa County General Hospital. Contact: H. F. Lenhardt, M.D., Dir. of Medical Education. Approved for category 1 credit.

The Hand Surgery Conference
Wednesday 7:30 a.m., Santa Cruz Room, Maricopa County Hospital.

MEMORIAL HOSPITAL

1201 S. 7th Ave., Phoenix, AZ 85036. Sponsor: Memorial Hospital. Approved for category 1 credit.

Month Medical Education Seminar
Third Monday, 6:30 p.m., Kiva Conference Rm. Contact: George Scharf, M.D.

Tumor Board Conference
Every Friday at Noon, Kiva Conference Rm. Contact: Howard Kimball, M.D.

SCOTTSDALE MEMORIAL HOSPITAL

7300 E. 4th St., Scottsdale, AZ 85251. Sponsor: Scottsdale Memorial Hospital. Contact: W. S. Wliams, M.D., Director of Medical Education

Clinical Pathological Conference
4th Monday, monthly, 12:45 p.m.

Family Practice Conference
1st Monday, monthly, 12:45 p.m.

Medical Grand Rounds
3rd Monday, monthly, 12:45 p.m.

Morbidity & Mortality Conference
2nd Monday, monthly, 12:45 p.m.

ST MARY'S HOSPITAL & HEALTH CENTER

1601 W. St. Mary's Rd., Tucson, AZ 85703. Sponsor: St. Mary's Hospital & Health Center. Contact: see below.

Cardiology Conference
Every Friday 8-9 a.m., Century Rm. A. Contact: Anthony L. Forte, M.D.

Monthly Specialty Conference of the Department of Surgery
First Monday, monthly, 7:30 a.m. Century Rm. A. Contact: Medical Staff Office. Approved for 1 hour of category 1 credit

Grand Rounds: Medical Surgical, Family Practice, Pathology, Radiology
Weekly, Thursday, 7-8:30 a.m. Contact: Richard A. Silver, M.D. Approved for 1 hours of category 1 credit.

U OF A HEALTH SCIENCES CENTER

Sponsor: U of A College of Medicine, Tucson, AZ 85724. Contact: See below. Approved for category 1 credit.

Clinical Immunology, Allergy & Rheumatology Rounds
Every Friday, Noon-1 p.m. Contact: John Boyer, M.D., Dept. of Internal Medicine.

Cerebrovascular Disease Conference
Mondays, 5-6 p.m., weekly, Rm. 5505. Contact: Wesly Moore, M.D.,Depts. of Surgery, Nurology & Radiology.

Dean's Clinical Rounds
Contact: Louis J. Kettel, M.D.

Endocrinology Seminar
Every Thursday, Noon-1 p.m., 1st, 3rd & 5th Thursday, Room N318, VA Hospital. 2nd & 4th Thursday, Room 6505, Tucson Medical Center. Contact: Dept. of Internal Medicine.

Hematology-Oncology Clinical Conferenc
Every Tuesday, Noon-1 p.m., 1st, 3rd & 5 Tuesdays, Rm 6505, Tucson Medical Cent 2nd & 4th Tuesdays, Rm. N318, VA Hospit Contact: Sidney Salmon, M.D., Dept. Internal Medicine.

Joint Thyroid Clinic Conference
1st & 3rd Mondays of every month. 1 to 2 p. AHSC,Rm. 6505. Contact: Sidney Wern M.D., Dept. of Internal Medicin Endocrinology Section.

Medical Grand Rounds
Every Wed., Noon-1p.m., 1st, 3rd, & 5th We Staff Conf. Room, VA Hospital. 2nd & 4 Wed.,Rm. 5403, UAHSC. Contact: Jay Smi M.D., Dept. of Internal Medicine.

Nuclear Medicine
Thursday, 7:30 a.m., Radiology Conf. R UAHSC. Contact: Irwin M. Freundlich, M. Dept. of Diagnostic Radiology.

Neurology Grand Rounds
Every Friday, Noon, 1st, 3rd, & 5th Frida UAHSC, Rm. 7505. 2nd & 4th Fridays, Hospital. Contact: William A. Sibley, M. Dept. of Neurology.

Neuropathology Review Conference
Thursdays, 8:30 a.m., Rm. 5120, UAHS Contact: Peter C. Johnson, M.D.

Neurosciences Seminar
Every Friday, 7:30 a.m.,UAHSC, Rm 75 Contact: Colin R. Bamford, M.D., or Jose Laguna, M.D., Dept. of Neurology.

Pathology Seminar
Friday, 4:30-5:30 p.m., Rm. 5120, UAHS Contact: Paul Finley, M.D., Dept. Pathology.

Tucson Pathologist Conference
First Monday of the Month, 7:30-9 p. Rotation between Tucson Pathology Co Rms. Contact: Anna Graham, M.D., Tucs Pathologists.

Pediatric Grand Rounds
Every Tuesday, 12:30-1:30 p.m. Alternat between Tucson Medical Center & UAHS Contact: Hugh Thompson, M.D., Dept. Pediatrics.

Problem Case Workshop
3rd Monday of each month, 7:30 a.m., 4410, UAHSC. Contact: H. E. Cross, M. Ph.D., Div. Of Ophthalmology.

Psychiatric Grand Rounds
Every Wednesday, Sept. to May 4, 5:30 p. Rm8403 UAHSC. Contact: Alan Levens M.D., Dept. of Psychiatry.

Chest Radiology
Monday, 5-6 p.m., weekly, Rm 153 UAHSC. Contact: Irwin M. Freundlich, M. Dept. of Radiology.

Gastrointestinal Radiology
Mondays, 7:30 a.m., weekly except summer months. Contact: Irwin Freundlich, M.D., Dept. of Radiology.

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CONTRAINDICATIONS: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components. Do not use in the eyes or in the external ear canal if the eardrum is perforated.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.

Radiation Oncology Planning Conference
Friday, weekly, 8:30-10 a.m., UAHSC, Rm. 0655. Contact: Robert S. Heusinkveld, M.D., Radiation Oncology Section.

Radiology-Rheumatology Conference
Thursday, 8 a.m., UAHSC, Library Rm.1535C. Contact: Irwin M. Freundlich, M.D. Dept. of Radiology.

Vascular Radiology
Radiology Interesting Case Conference
Thursday, Noon, VA Hospital. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Resident's Conference
Wednesday, weekly 5-6 p.m., Diag. Radiology Conf. Rm. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology

Trauma Conference
Every Thursday,4-5 p.m. UAHSC, Rm. 5505. Contact: Martin Silverstein, M.D., Dept. of Surgery.

Grand Ward Rounds—Trauma
Every Tuesday, 8 a.m., UAHSC. Contact: Martin Silverstein, Surgery Dept., Trauma Section.

Monthly Meeting Tucson
Ultrasonography Group
First Wed. of month, 4:30-5:30 p.m., UAHSC. Contact: Irwin M. Freundlich, M.D.

Tucson Urological Society
Scientific Meeting
Monthly. Contact: George W. Drach, M.D., Depts. of Surgery & Urology.

General Urology Conference
Tuesday 5-6 p.m. Thursday, Noon-1:30 p.m. UAHSC Meeting Rooms & VA Hospital. Contact: George W. Drach, M.D., Dept of Surgery/Urology Section.

VETERANS ADMINISTRATION HOSPITAL

7th St. and Indian School Rd., Phoenix, AZ 85012. Sponsor: VA Hospital. Contact: Jasper L. McPhail, M.D. Approved for Category 1 credit.

Academic Surgery Conference
Each Thursday — 2 p.m. — C435, Dr. Cannon, Ext. 493.

Cardiology Conference
2nd Thursday — 1 p.m. — T5, Dr. Habibzadeh, Ext. 348.

Cancer Symposium
Each Wednesday — 1 p.m. — T5, Dr. Berkley, Ext. 419.

Clinical Conference
4th Thursday of 3rd Month, (Mar. Jun., Sept., & Dec.), 1 p.m. — T5, Dr. Likos, Ext. 623.

Dermatology Conference
1st, 2nd, & 3rd Wednesday (usually, but is subject to change) 10 a.m. — C118, Dr. Roberts, Ext. 426.

G.I. Radiology Clinical Correlation Conference 1st & 3rd Monday — 1 p.m. — C435, Dr. Sanowski, Ext. 618.

G.I. Grand Rounds
Ech Tuesday — 1 p.m. — T5, (4th Thursday with U of A Consultants) Dr. Sanowski, Ext. 618.

Medical Service Grand Rounds
Each Friday — 11 a.m. — T5, Dr. Zeller, Ext 272

Medical-Surgical Chest Conference
1st and 3rd Thursday — 1 p.m. — T5, Dr. Chowdhury, Ext. 388.

Medical-Surgical G.I. Conference
Ist & 3rd Friday — 2 p.m. — 2123, Dr. Sanowski, Ext. 618.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery-Pathology Conference
Each Thursday — 2 p.m. — 2128, Dr. Cannon, Ext 493, & Dr. Likos, Ext. 623.

Urology-Pathology Conference
Each Wednesday — 7 a.m. — 2128, Dr. Likos, Ext. 623 & Dr. Pentenney, Ext., 417.

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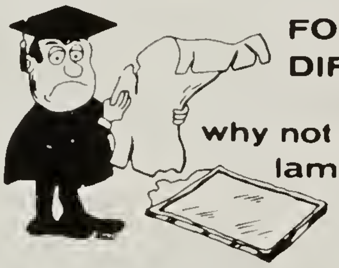

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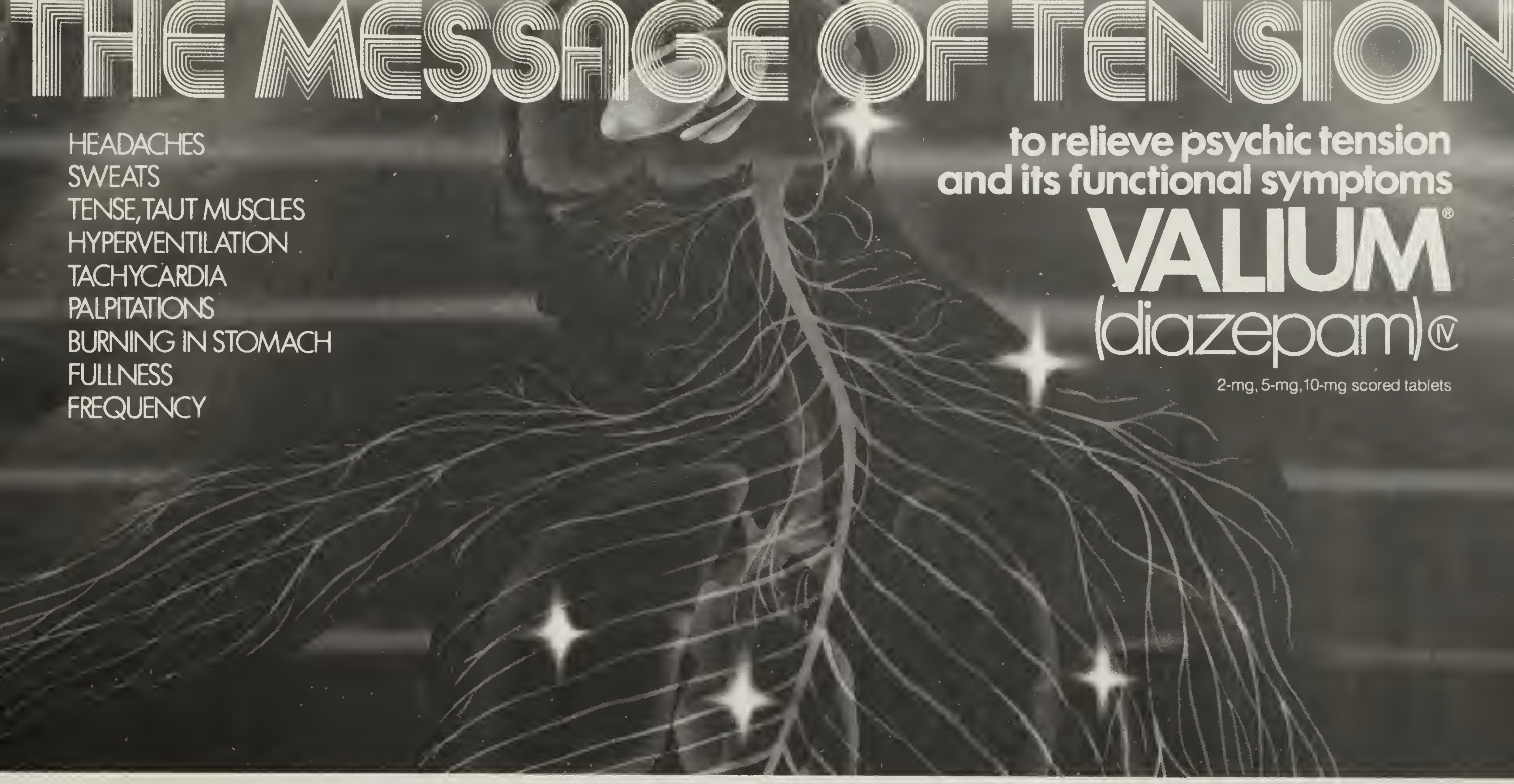

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***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**
Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed, drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.
Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported, should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Efficacy of MONISTAT i.v. therapy...

highly favorable rates of recovery or clinical improvement

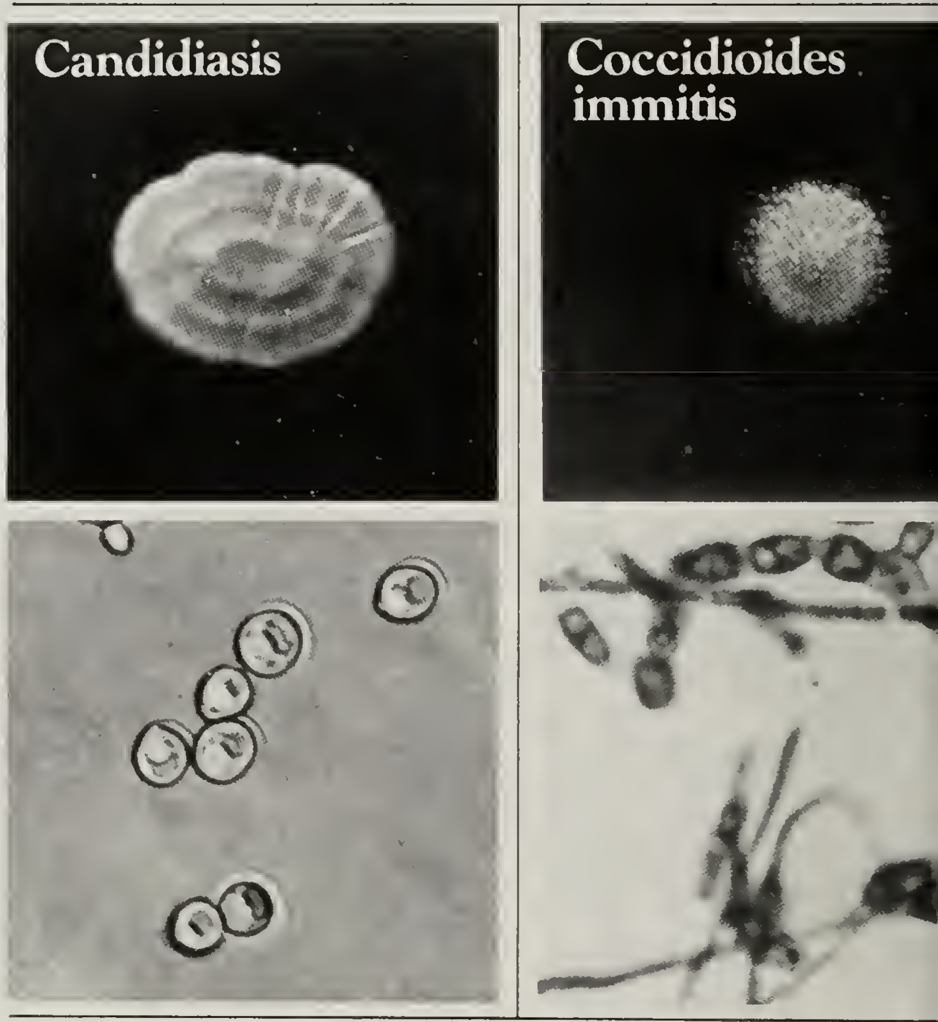
- effective against systemic candidiasis
  - chronic mucocutaneous candidiasis
  - coccidioidomycosis
  - cryptococcosis
  - paracoccidioidomycosis
- in patients who did not respond to amphotericin B therapy
- in immunologically-compromised patients with severe infections

rapid onset of clinical improvement

In most patients who responded, improvement was observed within 1-3 weeks of MONISTAT i.v. therapy; however, prolonged treatment courses may be necessary to prevent relapse.

no development of fungal resistance during therapy reported

In vitro resistance of clinical isolates has not been observed during clinical trials.



Photos courtesy of Dubos, J. R., Bacterial and Mycotic Infections of Man, J. B. Lippincott Company, 1968 and Burrows, W., Textbook of Microbiology, W. B. Saunders Company, 19th edition.

and the side effect profile

no nephrotoxicity or other permanent adverse effects in clinical studies

- even in prolonged therapy
- even in patients with renal disease

extensively evaluated

During clinical trials in over 400 patients, no permanent adverse reactions were reported.

Adverse reactions

MONISTAT i.v. should not be administered undiluted. Rapid injection of the undiluted solution may produce transient tachycardia or arrhythmia.

Adverse reactions include phlebitis, pruritus, rash, nausea, vomiting, febrile reactions, drowsiness, diarrhea, anorexia and flushes. Transient hematologic changes have occurred; therefore, the patient should be closely monitored.

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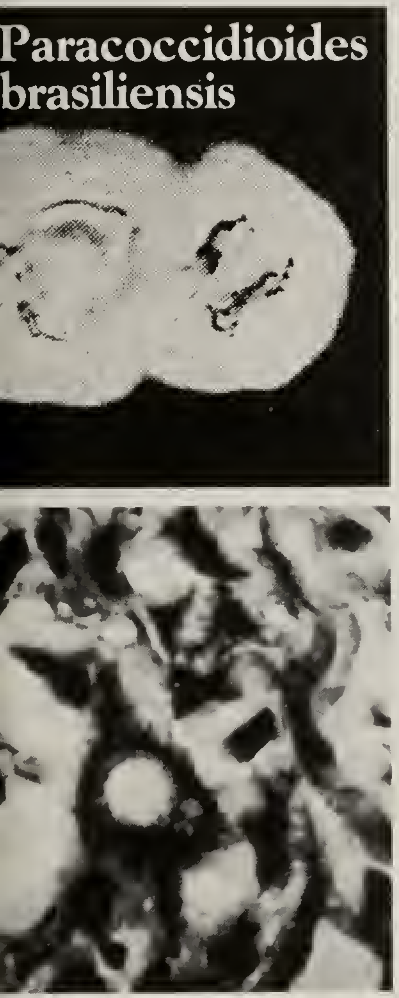
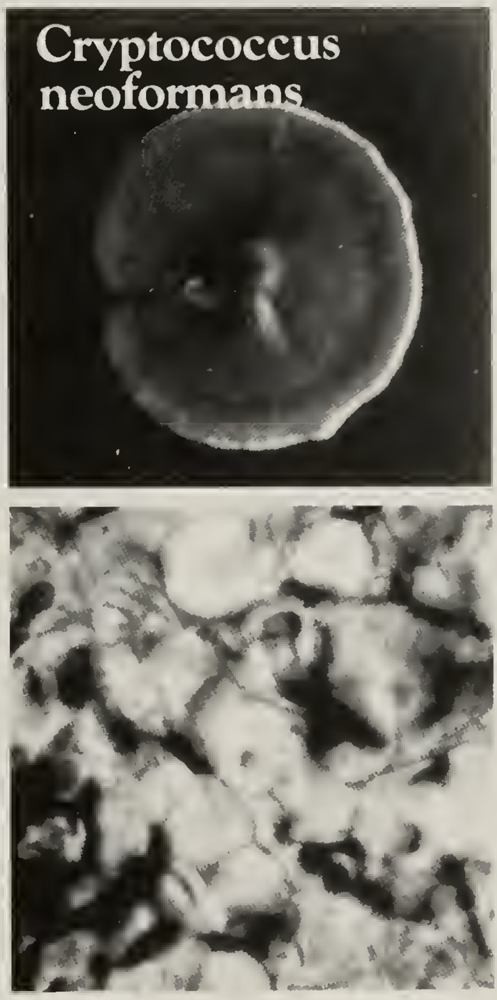
advancement
systemic mycoses





generally well tolerated by severely debilitated patients

- cancer patients
- patients receiving immunosuppressive drugs
- patients with serious underlying conditions such as renal insufficiency or diabetes mellitus

for more information

Because of the uniqueness of new MONISTAT i.v. only some of the highlights can be presented in this advertisement. For more information, i.e., product monograph, dosage schedules, etc., please fill out the coupon on the next page and mail to Ortho Pharmaceutical Corporation.

Please turn page for Prescribing Information

Ortho
Ortho Pharmaceutical Corporation
Raritan, New Jersey 08869

new
Monistat i.v.
TRADEMARK
(miconazole)

broad-spectrum activity against major systemic fungal pathogens

in systemic fungal infections...

new Monistat i.v.

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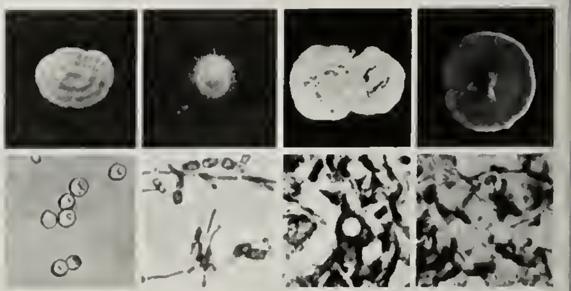
(miconazole)



a broad-spectrum systemic antifungal agent

DESCRIPTION: MONISTAT i.v. (miconazole) 1-{2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl) methoxyl ethyl} 1 H-imidazole is a synthetic antifungal supplied as a sterile solution for intravenous infusion. Each ml of this solution contains 10 mg of miconazole with 0.115 ml PEG 40 castor oil, 1.0 mg lactic acid USP, 0.5 mg methylparaben USP, 0 05 mg propylparaben USP in water for injection. Miconazole i.v. is a clear, colorless to slightly yellow solution having a pH of 3.7 to 5.7.

CLINICAL PHARMACOLOGY: MONISTAT i.v. is rapidly metabolized in the liver and about 14% to 22% of the administered dose is excreted in the urine, mainly as inactive metabolites. The pharmacokinetic profile fits a three-compartment open model with the following biologic half-life: 0 4, 2.1, and 24.1 hours for each phase respectively. The pharmacokinetic profile of MONISTAT i v is unaltered in patients with renal insufficiency, including those patients on hemodialysis. The in/vitro antifungal activity of MONISTAT i v. is very broad Clinical efficacy has been demonstrated in patients with the following species of fungi: *Coccidioides immitis*, *Candida albicans*, *Cryptococcus neoformans*, *and Paracoccidioides brasiliensis*.

Recommended doses of MONISTAT i.v. produce serum concentrations of drug which exceed the in-vitro MIC values for the fungal species noted above. Doses above 9 mg/kg of MONISTAT i.v produce peak blood levels above 1 μg/ml in most cases. The drug penetrates into joints.

INDICATIONS: MONISTAT i.v. is indicated for the treatment of the following severe systemic fungal infections. coccidioidomycosis, candidiasis, cryptococcosis, paracoccidioidomycosis, and for the treatment of chronic mucocutaneous candidiasis. However, in the treatment of fungal meningitis and urinary bladder infections an intravenous infusion alone is inadequate. It must be supplemented with intrathecal administration and bladder irrigation. Appropriate diagnostic procedures should be followed and MICs should be determined

MONISTAT i.v. should not be used to treat common trivial forms of fungal diseases.

CONTRAINDICATIONS: MONISTAT i.v. is contraindicated in those patients who have shown hypersensitivity to it.

WARNINGS: Rapid injection of undiluted MONISTAT i.v , may produce transient tachycardia or arrhythmia

PRECAUTIONS: Before a treatment course of MONISTAT i.v. is started, the physician should make sure that the patient is not hypersensitive to the drug product MONISTAT i.v should be given by intravenous infusion. The treatment should be started under stringent conditions of hospitalization but subsequently may be given to suitable patients under ambulatory conditions with close clinical monitoring It is recommended that an initial dose of 200 mg be given with the physician in attendance. It is also recommended that clinical laboratory monitoring including hemoglobin, hematocrit, electrolytes and lipids be performed.

It should be borne in mind that systemic fungal mycoses may be complications of chronic underlying conditions which in themselves may require appropriate measures.

Pregnancy: Reproductive studies with MONISTAT i v. in rats and rabbits revealed no evidence of impaired fertility or harm to the fetus. There are no data, however, on the use of the drug in pregnant women.

Children: Since the safety of miconazole i.v in children under one year of age has not been extensively studied, its benefits in this age group must be weighed against the possible risks involved

ADVERSE REACTIONS: Adverse reactions which have been observed with MONISTAT i.v. therapy include phlebitis, pruritus, rash, nausea, vomiting, febrile reactions, drowsiness, diarrhea, anorexia and flushes. In the U.S. studies, 29% of 209 patients studied had phlebitis, 21% pruritus, 18% nausea, 10% fever and chills, 9% rash, and 7% emesis. Transient decreases in hematocrit and serum sodium values have been observed following infusion of MONISTAT i.v. Thrombocytopenia has also been reported No serious renal or hepatic toxicity has been reported If pruritus and skin rashes are severe, discontinuation of treatment may be necessary. Nausea and vomiting can be mitigated with antihistaminic or antiemetic drugs given prior to MONISTAT i.v. infusion, or by reducing the dose, slowing the rate of infusion, or avoiding administration at mealtime.

Aggregation of erythrocytes or rouleau formation on blood smears has been reported Hyperlipemia has occurred in patients and is reported to be due to the vehicle. Cremophor EL (PEG 40 castor oil).

DRUG INTERACTIONS: Drugs containing cremophor-type vehicles are known to cause electrophoretic abnormalities of the lipoprotein. These effects are reversible upon discontinuation of treatment but are usually not an indication that treatment should be discontinued.

Interaction with the coumarin drugs resulting in an enhancement of the anticoagulant effect has also been reported In cases of simultaneous treatment with MONISTAT i.v and coumarin drugs, the anticoagulant effect should be carefully titrated since reductions of the anticoagulant doses may be indicated

DOSAGE AND ADMINISTRATION

DOSAGE

Adults. The doses may vary with the diagnosis and with the infective agent, from 200 to 1200 mg per infusion The following daily doses, which may be divided over 3 infusions, are recommended:

Organism	Dosage Range*	Duration of Successful Therapy (weeks)
Coccidioidomycosis:	1800 to 3600 mg per day	3 to > 20
Cryptococcosis:	1200 to 2400 mg per day	3 to > 12
Candidiasis:	600 to 1800 mg per day	1 to > 20
Paracoccidioidomycosis:	200 to 1200 mg per day	2 to > 16

*May be divided over 3 infusions.

Repeated courses may be necessitated by relapse or reinfection.

Children: A total daily dose of about 20 to 40 mg/kg is generally adequate. However, a dose of 15 mg/kg body weight per infusion should not be exceeded.

ADMINISTRATION: MONISTAT i.v. should be diluted in at least 200 ml of fluid. The diluent of choice is 0.9% sodium chloride or alternatively Dextrose 5% injectable solution. The intravenous infusion should be given over a period of 30 to 60 minutes.

Generally, treatment should be continued until all clinical and laboratory tests no longer indicate that active fungal infection is present. Inadequate periods of treatment may yield poor response and lead to early recurrence of clinical symptoms. The dosing intervals and sites and the duration of treatment vary from patient to patient and depend on the causative organism.

OTHER MODES OF ADMINISTRATION: Intrathecal. Administration of the undiluted injectable solution of MONISTAT i.v. by the various intrathecal routes (20 mg per dose) is indicated as an adjunct to intravenous treatment in fungal meningitis. Succeeding intrathecal injections may be alternated between lumbar, cervical, and cisternal punctures every 3 to 7 days. Bladder instillation of 200 mg of diluted solution is indicated in the treatment of mycoses of the urinary bladder.

HOW SUPPLIED: MONISTAT i.v. is supplied in 20 ml ampoules.

MONISTAT i.v. (miconazole) is an original product of Janssen Pharmaceutica N V., Belgium, and co-developed by Ortho Pharmaceutical Corporation.

Ortho Pharmaceutical Corporation
Raritan, New Jersey 08869

Ortho Pharmaceutical Corporation **AM 5-79**
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Please send me more information on the new broad-spectrum, systemic antifungal agent... MONISTAT i.v. (miconazole).

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Minimum Lease Agreement	3 years
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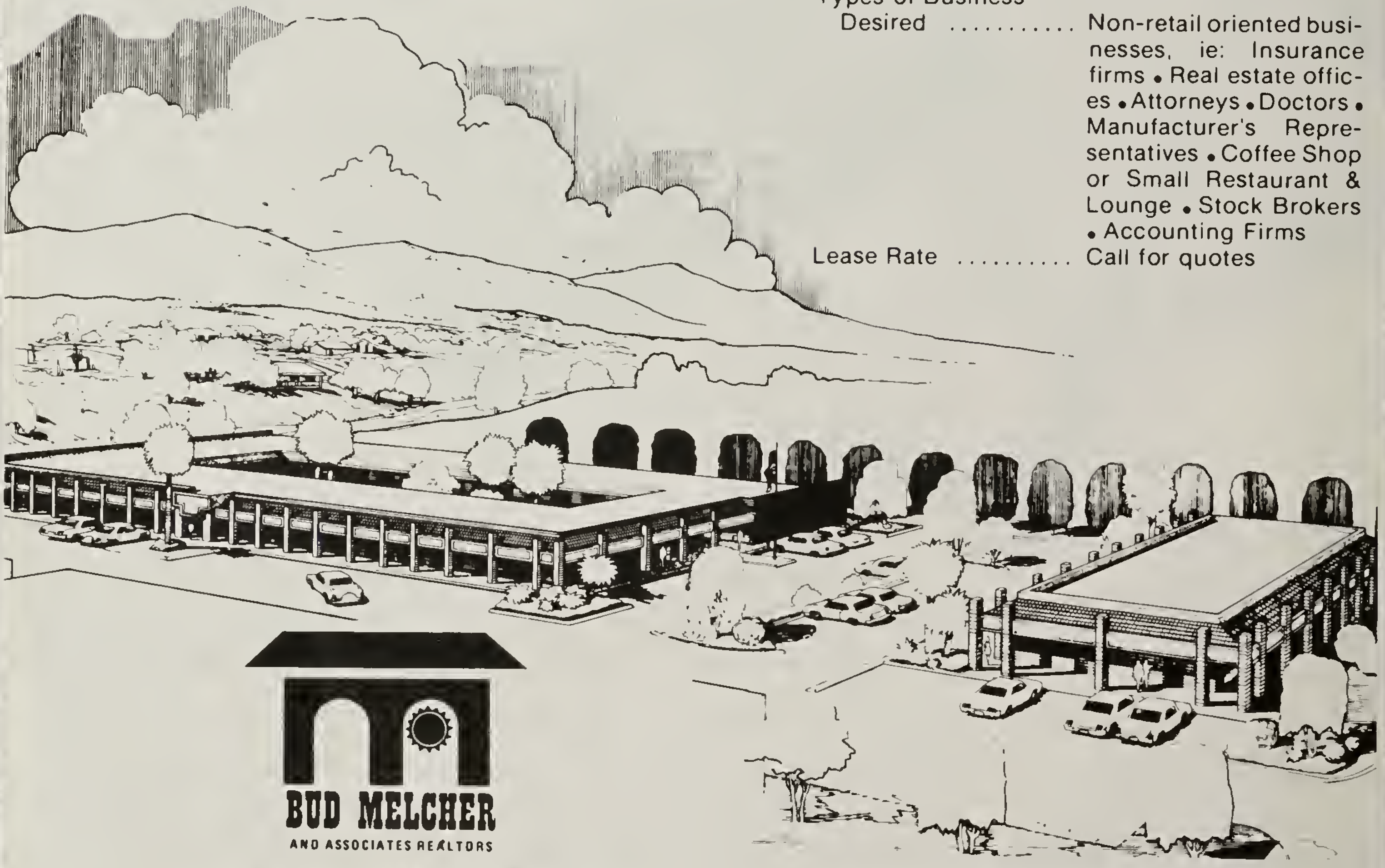
Types of Business Desired	Non-retail oriented businesses, ie: Insurance firms • Real estate offices • Attorneys • Doctors • Manufacturer's Representatives • Coffee Shop or Small Restaurant & Lounge • Stock Brokers • Accounting Firms
Lease Rate	Call for quotes



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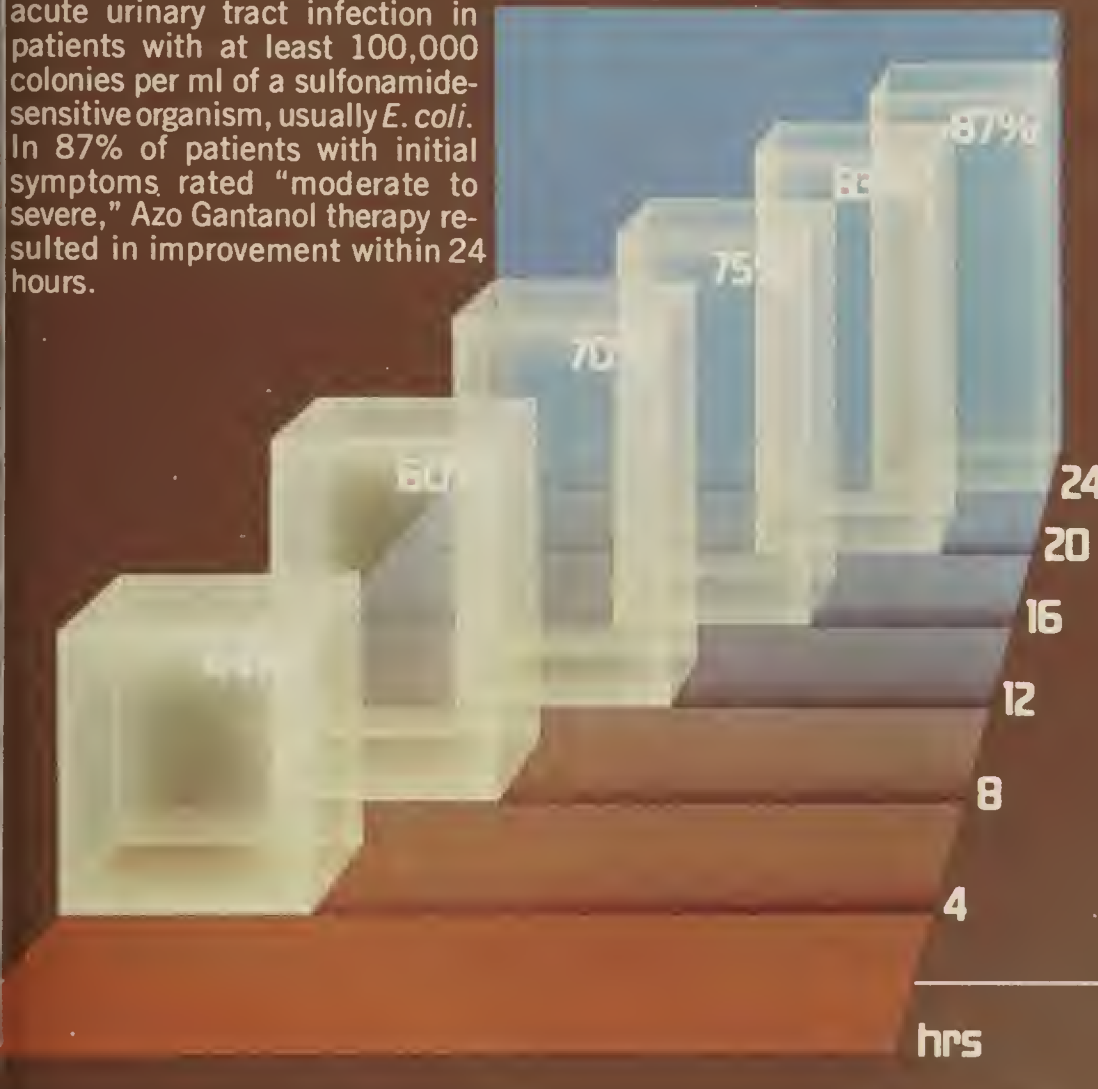
A controlled, multicenter study assessed the efficacy of Azo Gantanol in relieving pain and/or burning associated with acute urinary tract infection in patients with at least 100,000 colonies per ml of a sulfonamide-sensitive organism, usually *E. coli*. In 87% of patients with initial symptoms rated "moderate to severe," Azo Gantanol therapy resulted in improvement within 24 hours.



Fast pain relief plus effective antibacterial action

Azo Gantanol®

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

for the pain **for the pathogens**

*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Preteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

Warnings: Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

Supplied: Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

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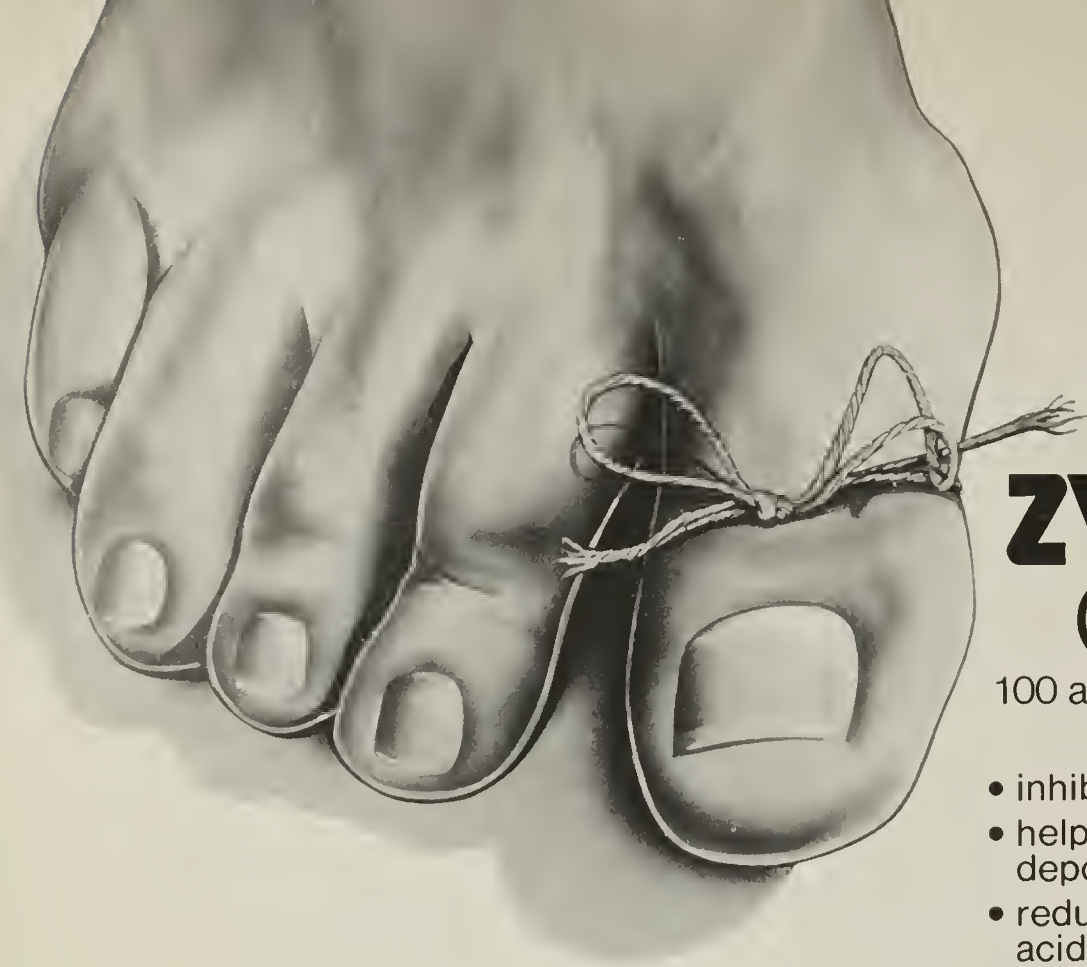
Nutley, New Jersey 07110



A reminder

ZYLOPRIM®

(allopurinol)

100 and 300 mg scored Tablets

- inhibits uric acid formation
- helps prevent urate crystal depositions in synovia
- reduces risk of uric acid lithiasis

INDICATIONS AND USE: This is not an innocuous drug and strict attention should be given to the indications for its use. Pending further investigation, its use in other hyperuricemic states is not indicated at this time.

Zyloprim® (allopurinol) is intended for:

1. treatment of gout, either primary, or secondary to the hyperuricemia associated with blood dyscrasias and their therapy;
2. treatment of primary or secondary uric acid nephropathy, with or without accompanying symptoms of gout;
3. treatment of patients with recurrent uric acid stone formation;
4. prophylactic treatment to prevent tissue urate deposition, renal calculi, or uric acid nephropathy in patients with leukemias, lymphomas and malignancies who are receiving cancer chemotherapy with its resultant elevating effect on serum uric acid levels.

CONTRAINDICATIONS: Use in children with the exception of those with hyperuricemia secondary to malignancy. The drug should not be employed in nursing mothers.

Patients who have developed a severe reaction to Zyloprim should not be restarted on the drug.

WARNINGS: ZYLOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR ANY SIGN OF ADVERSE REACTION. In some instances a skin rash may be followed by more severe hypersensitivity reactions such as exfoliative, urticarial and purpuric lesions as well as Stevens-Johnson syndrome (erythema multiforme) and very rarely a generalized vasculitis which may lead to irreversible hepatotoxicity and death.

A few cases of reversible clinical hepatotoxicity have been noted and in some patients asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. Accordingly, periodic liver function tests should be performed during the early stages of therapy, particularly in patients with pre-existing liver disease.

Patients should be alerted to the need for due precautions when engaging in activities where alertness is mandatory.

Nevertheless, iron salts should not be given simultaneously with Zyloprim. This drug should not be administered to immediate relatives of patients with idiopathic hemochromatosis.

In patients receiving Purinethol® (mercaptopurine) or Imuran® (azathioprine), the concomitant administration of 300-600 mg of Zyloprim per day will require a reduction in dose to approximately one-third to one-fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of Purinethol or Imuran should be made on the basis of therapeutic response and any toxic effects.

Usage in Pregnancy and Women of Childbearing Age: Zyloprim® (allopurinol) should be used in pregnant women or women of childbearing age only if the potential benefits to the patient are weighed against the possible risk to the fetus.

PRECAUTIONS: Some investigators have reported an increase in acute attacks of gout during the early stages of allopurinol administration, even when normal or subnormal serum uric acid levels have been attained.

It has been reported that allopurinol prolongs the half-life of the anticoagulant, dicumarol. This interaction should be kept in mind when allopurinol is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

A fluid intake sufficient to yield a daily urinary output of at least 2 liters and the maintenance of a neutral or, preferably, slightly alkaline urine are desirable to (1) avoid the theoretic possibility of formation of xanthine calculi under the influence of Zyloprim therapy and (2) help prevent renal precipitation of urates in patients receiving concomitant uricosuric agents.

Patients with impaired renal function require less drug and should be carefully observed during the early stages of Zyloprim administration and the drug withdrawn if increased abnormalities in renal function appear.

In patients with severely impaired renal function, or decreased urate clearance, the half-life of oxipurinol in the plasma is greatly prolonged. Therefore, a dose of 100 mg per day or 300 mg twice a week, or perhaps less, may be sufficient to maintain adequate xanthine oxidase inhibition to reduce serum urate levels. Such patients should be treated with the lowest effective dose, in order to minimize side effects.

Mild reticulocytosis has appeared in some patients.

As with all new agents, periodic determination of liver and kidney function and complete blood counts should be performed especially during the first few months of therapy.

ADVERSE REACTIONS:

Dermatologic: Because in some instances skin rash has been followed by severe hypersensitivity reactions, it is recommended that therapy be discontinued at the first sign of rash or other adverse reaction (see WARNINGS). Skin rash, usually maculopapular, is the adverse reaction most commonly reported.
Exfoliative, urticarial and purpuric lesions, Stevens-Johnson syndrome (erythema multiforme) and toxic epidermal necrolysis have also been reported.
A few cases of alopecia with and without accompanying dermatitis have been reported.
In some patients with a rash, restarting Zyloprim (allopurinol) therapy at lower doses has been accomplished without untoward incident.

Gastrointestinal: Nausea, vomiting, diarrhea, and intermittent abdominal pain have been reported.

Vascular: There have been rare instances of a generalized hypersensitivity vasculitis or necrotizing angiitis which have led to irreversible hepatotoxicity and death.

Hematopoietic: Agranulocytosis, anemia, aplastic anemia, bone marrow depression, leukopenia, pancytopenia and thrombocytopenia have been reported in patients, most of whom received concomitant drugs with potential for causing these reactions. Zyloprim® (allopurinol) has been neither implicated nor excluded as a cause of these reactions.

Neurologic: There have been a few reports of peripheral neuritis occurring while patients were taking Zyloprim. Drowsiness has also been reported in a few patients.

Ophthalmic: There have been a few reports of cataracts found in patients receiving Zyloprim. It is not known if the cataracts predated the Zyloprim therapy. "Toxic" cataracts were reported in one patient who also received an anti-inflammatory agent; again, the time of onset is unknown. In a group of patients followed by Gutman and Yü for up to five years on Zyloprim therapy, no evidence of ophthalmologic effect attributable to Zyloprim was reported.

Drug Idiosyncrasy: Symptoms suggestive of drug idiosyncrasy have been reported in a few patients. This was characterized by fever, chills, leukopenia or leukocytosis, eosinophilia, arthralgias, skin rash, pruritus, nausea and vomiting.

OVERDOSAGE: Massive overdosing, or acute poisoning, by Zyloprim has not been reported.

HOW SUPPLIED: 100 mg (white) scored tablets, bottles of 100 and 1000; 300 mg (peach) scored tablets, bottles of 30, 100 and 500. Unit dose packs for each strength also available.

Complete information available from your local B. W. Co. Representative or from Professional Services Department PML.

U.S. Patent No. 3,624,205 (Use Patent)

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- Vasodilan—compatible with concomitant therapy
- Vasodilan—compatible with your total regimen for vascular insufficiency

*__Indications:__ Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, the FDA has classified the indications as follows·

Possibly Effective

1 For the relief of symptoms associated with cerebral vascular insufficiency
2 In peripheral vascular disease of arteriosclerosis obliterans, thromboangiitis obliterans (Buerger's Disease) and Raynaud's disease.

Final classification of the less-than-effective indications requires further investigation.

Composition: Vasodilan tablets, isoxsuprine HCl, 10 mg and 20 mg.
Vasodilan injection, isoxsuprine HCl, 5 mg., per ml.

Dosage and Administration: Oral· 10 to 20 mg., three or four times daily
Intramuscular· 5 to 10 mg.(1 or 2 ml.) two or three times daily Intramuscular administration may be used initially in severe or acute conditions

Contraindications and Cautions: There are no known contraindications to oral use when administered in recommended doses Should not be given immediately postpartum or in the presence of arterial bleeding

Parenteral administration is not recommended in the presence of hypotension or tachycardia

Intravenous administration should not be given because of increased likelihood of side effects.

Adverse Reactions: On rare occasions oral administration of the drug has been associated in time with the occurrence of hypotension, tachycardia, nausea, vomiting, dizziness, abdominal distress, and severe rash. If rash appears the drug should be discontinued

Although available evidence suggests a temporal association of these reactions with isoxsuprine, a causal relationship can be neither confirmed nor refuted.

Administration of single dose of 10 mg. intramuscularly may result in hypotension and tachycardia These symptoms are more pronounced in higher doses For these reasons single intramuscular doses exceeding 10 mg. are not recommended Repeated administration of 5 to 10 mg. intramuscularly at suitable intervals may be employed.

Supplied: Tablets, 10 mg., bottles of 100, 1000, 5000 and Unit Dose, Tablets, 20 mg., bottles of 100, 500, 1000, 5000 and Unit Dose, Injection, 10 mg. per 2 ml ampul, box of six 2 ml. ampuls

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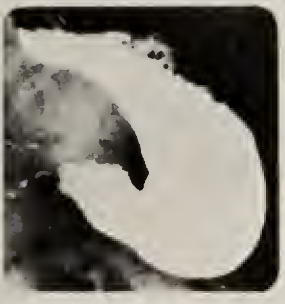
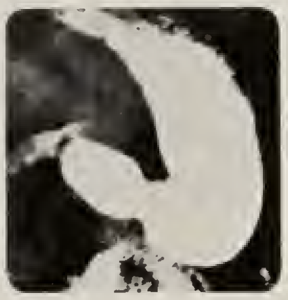
In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.


Pylorospasm has almost totally blocked passage of barium meal.


Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:
King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

Merrell

B-4420 (Y736A) MNR-804

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Capsules, Tablets, Syrup, Injection

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary

INDICATIONS
Based on a review of this drug by the National Academy of Sciences–National Research Council and/or other information, FDA has classified the following indications as "probably" effective.

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. WARNINGS: In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug PRECAUTIONS: Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy Use with caution in patients with: Autonomic neuropathy. Hepatic or renal disease Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. ADVERSE REACTIONS: Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention, blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia, nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling, severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation DOSAGE AND ADMINISTRATION Dosage must be adjusted to individual patient's needs

Usual Dosage: Bentyl 10 mg. capsule and syrup: *Adults* 1 or 2 capsules or teaspoonfuls syrup three or four times daily *Children* 1 capsule or teaspoonful syrup three or four times daily. *Infants* ½ teaspoonful syrup three or four times daily (May be diluted with equal volume of water.) Bentyl 20 mg.: *Adults*: 1 tablet three or four times daily Bentyl Injection. *Adults* 2 ml. (20 mg.) every four to six hours intramuscularly only NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE: The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation Treatment should consist of gastric lavage, emetics, and activated charcoal Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine™ (bethanecol chloride USP) should be used.

Product Information as of October, 1978.

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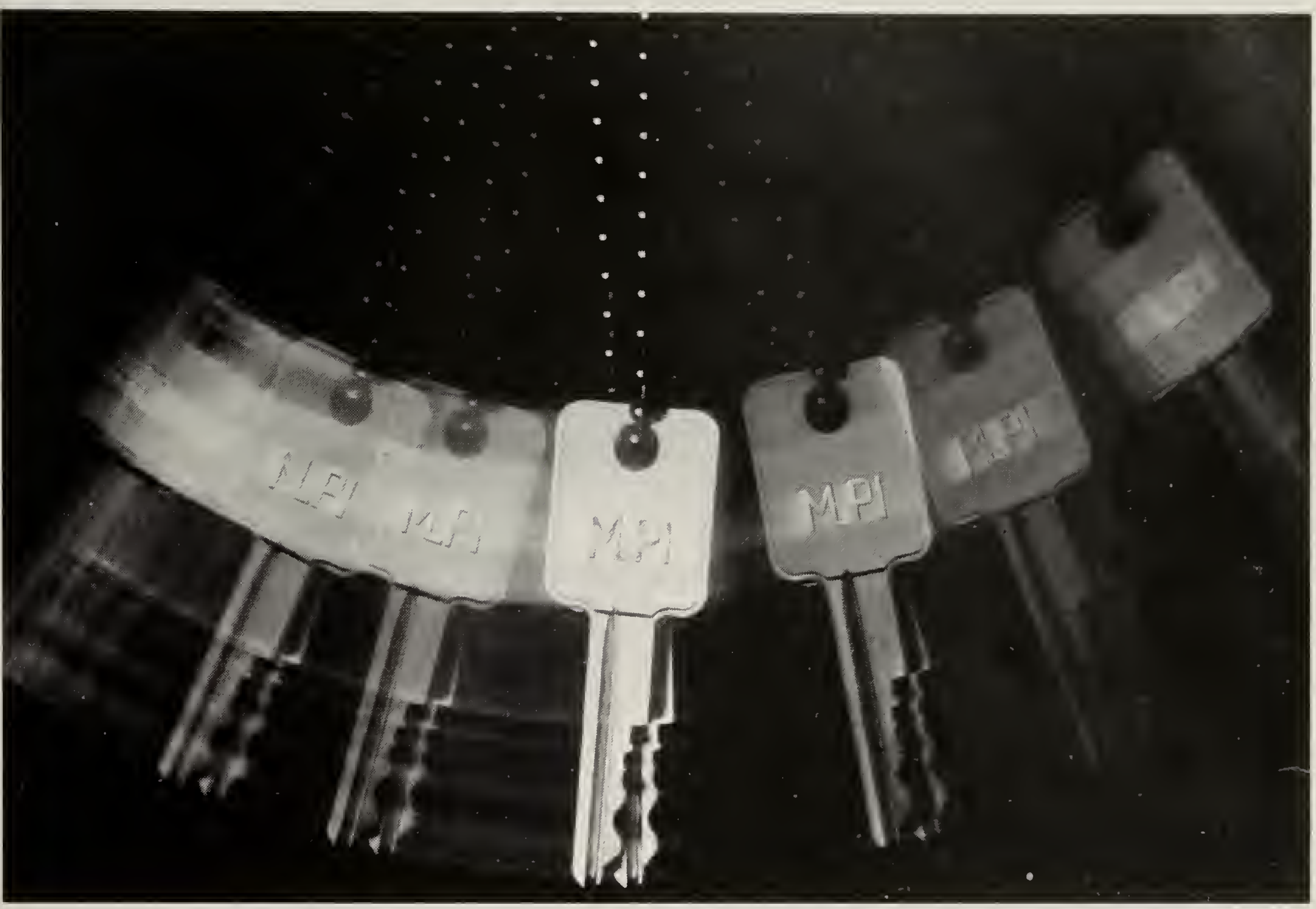

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The Maker

Examining a Few Myths About Prescribing.

Increasing pressure is being put on the practicing physician to prescribe drugs generically. You are told that brand–name products are universally "expensive" and generic versions are relatively "cheap." To make this case, the most extreme (rather than typical) price differentials are cited. Thus, consumers are led to believe that such differentials are commonplace. Even your knowledge and your motives as a physician are questioned.

Understandably, these views have created myths. We think it's time to examine them in the light of all the facts and ramifications.

MYTH: There are no differences in quality and performance between brand-name products and their generic counterparts. The corollary is that there are no differences among products made by high-technology, quality-conscious, research-based companies and those made by commodity-type suppliers.

FACT: The Food and Drug Administration does a good job in monitoring a generally excellent drug supply. Still, it has nowhere near the resources to guarantee the quality and bioavailability of all marketed products at any given time. Just a few months ago, for example, it noted that batches of tetracycline HCl capsules which met official monograph requirements were not bioequivalent to a reference product. As you know, there is substantial literature on this subject affecting many drugs, including such antibiotics as tetracycline and erythromycin. The record on drug recalls and court actions affirms strongly that there are differences among pharmaceutical companies and their products. Research-intensive companies have far better records than those that do no research and may practice minimum quality assurance.

MYTH: Industry favors only "expensive" brand names and denigrates all generics.

FACT: PMA companies make 90 to 95 percent of the drug supply, including, therefore, most of the generics. Drug nomenclature is not the important point; it's the competence of the manufacturer and the integrity of the product that count.

Matters.

MYTH: Generic options almost always exist.

FACT: About 55 percent of prescription drug expenditure is for single-source drugs. This means, of course, that for only 45 percent of such expenditure, is a generic prescribing option available.

MYTH: Generic prescriptions are filled with inexpensive generics, thus saving consumers large sums of money.

FACT: Market data show that you invariably prescribe—and pharmacists dispense—both brand and generically labeled products from known and trusted sources, in the best interest of patients. In most cases the patient receives a proven brand product. Savings from voluntary or mandated generic prescribing are grossly exaggerated.

MYTH: Drugs account for a major portion of the rise in health care costs.

FACT: Drugs represent a very small part of such costs. The amount of the health care dollar spent for prescription drugs was about 12 cents in 1967; today it is about 8 cents. And you as a physician are most conscious of how drug therapy can cut hospitalization, avert surgery, reduce office visits and keep patients on the job.

MYTH: Government intrusions into the marketplace will save tax money.

FACT: Government schemes always cost the taxpayer something, and the costs often exceed the benefits. Certainly, any federal "help," such as lists of wholesale drug prices sent to all physicians and pharmacists, will be no exception. Just think of the expense of keeping them current! Moreover, wholesale prices are poor guides to actual transaction prices and even worse guides to retail prices.

The PMA Position

We believe your freedom to prescribe, either by generic or brand name, should be totally unabridged. Otherwise, your prescribing prerogatives and your relationships with patients will be seriously impaired.

The maker does matter

After the myths about price and equivalency have been shattered, one fact stands out more clearly than ever: *The maker does matter.* As always, your best guide to drug therapy for your patients is to select products—both brands and generics—from manufacturers with credentials and performance records you have come to respect.

PMA

Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

THE CHICAGO DEPARTMENT OF HEALTH

NEWS LETTER

VOL. 18, NO. 1, MAY, 1978

AUTOMATIC BLOOD PRESSURE DEVICES

A Chicago Department of Health report on the Vita-Stat automated blood pressure machines concludes that their consistency and accuracy is sufficient for screening purposes.

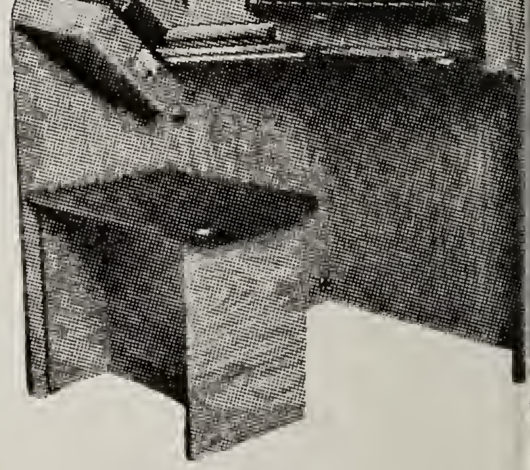
The report, the first in the nation based on a scientific study by a public agency, was prepared under the direction of Dr. David M. Berkson, the Department's heart disease control officer. It consists of (1) a statistical evaluation by Drs. Shekelle and Raynor of Rush-Presbyterian St. Luke's Medical Center, based on data collected over a four month period by Lawrence Shireman and Thomas Whipple and their co-workers in the Health Department, and (2) an evaluation of the results with recommendations for regulatory actions if deemed necessary. The report notes at the outset that any assessment of automatic blood pressure devices must compare their measurements with measurements by trained observers recorded by the traditional cuff ausculatory method. Since blood pressure may vary rapidly, the assessment of accuracy of measurement is difficult.

"In our evaluation of the Vita-Stat machine," the report states, "we found that, when the machine and a trained observer measure blood pressure simultaneously, there is a very good agreement." It is essential, however, that a machine must perform well in sequential measurement with trained observers as well as in simultaneous measurement. In sequential measurement the machine, in general, has a fair degree of accuracy. It does not perform as well, however, as trained technicians. In the laboratory analysis of the comparison between one machine and several technicians the machine tended to read systolic pressure 3.4mm higher and diastolic pressure 2.3mm lower. In the field analysis the machine tended to read systolic blood pressure 1.5mm and diastolic pressure 0.5mm higher than the technicians.

Although agreement between technicians in mean blood pressure measurement and in categorizing persons as normal, borderline or hypertensive tends to be closer than technician-machine agreement, these differences are small and of little practical significance in screening.

The report recommends that if licensing is insituted by the City of Chicago, periodic recalibration and testing should be required. The public must be informed that these instruments serve merely as screening devices; that they do not replace medical consultation and that, because blood pressure is subject to variation, several elevations or lack of elevations do not constitute a diagnosis of hypertension or normotension.

Blood pressure readings must be interpreted by a qualified medical professional and self-adjustment of medication based on automated blood pressure readings without medical supervision may be dangerous. The report concludes "that although the Vita-Stat machine does not perform as well as trained technicians, its consistency and accuracy is sufficient for screening purposes."



Accent on Education

Anthony F. Vuturo, M.D.

The University of Arizona College of Medicine is pleased to continue its tradition of submitting scientific articles to *Arizona Medicine* for publication in the annual College of Medicine issue. The unique contributions of the faculty of the College of Medicine to the science of medicine and ultimately to the people of Arizona are amply illustrated. Improved techniques in diagnosis and treatment in a short period of time have come from the nidus of conceptualization to the operational element of actualization. In essence, this is among the important contributions that the College of Medicine makes to the state and its citizens.

The articles selected for the physician audience of *Arizona Medicine* have at their conceptual base a firm understanding of the basic sciences. The application of advances in the basic sciences translated to clinical application is at the heart of the medical education process. The critical appraisal of meaningful advances for the patient is taught, not only in the laboratory, but more importantly, at the bedside.

It is expected that as continued significant advances are developed by the faculty at the College of Medicine they will quickly be disseminated to the practicing physician through continuing medical education techniques. While a great deal of attention is brought to bear on the more glamorous educational offerings such as international conferences and conventions, the primary vehicle for continuing self learning is through the physician's access to the articles appearing in the world body of medical literature. To this end, the College of Medicine contributes, again to this issue of *Arizona Medicine*.

From: University of Arizona College of Medicine, Office of Continuing Medical Education and Outreach, (Dr. Vuturo, Associate Dean).

Use of Electron Microscopy in Mycosis Fungoides and Other Cutaneous Oncologic Conditions

Robert Allen Schwartz, M.D., M.P.H.
Jerry L. Bangert, M.D.

Cutaneous oncology including the use of electron microscopic analysis has been well summarized.[1] [2] The use of electron microscopy in academically oriented dermatologic oncology has proliferated greatly. Although most of its use is investigational, there are a few contexts in which it can be of clinical value. We shall discuss its use in T-cell lymphomas (mycosis fungoides and the Sezary syndrome) and in hairy cell leukemia before mentioning other ways it may be of potential clincial value. It should be remembered that electron microscopy, like light microscopy, must be correlated with the gross pathology (the clinical lesion in dermatology) in order to be fully appreciated.

Mycosis Fungoides

Mycosis fungoides and its leukemic variant, the Sezary syndrome, are types of cutaneous T-cell lymphomas which spread to visceral organs and are often fatal. With the indentification of so-called Sezary or mycosis cells with both light and electron microscopy, the diagnosis of this important malignancy is facilitated. These cells appear about three times the size of erythrocytes and contain on electron microscopic examination a bizarrely shaped, convoluted nucleus often termed cerebriform (Fig. 1). They are also easily recognizable on routine Giemsa or Wright-stained blood smears, although the examination of the peripheral blood buffy coat is more likely to concentrate them and facilitate both light and electron microscopic recognition. In tissue specimens, the light microscopic views of plaque and tumor stage mycosis fungoides are usually either highly suggestive or in fact diagnostic. However, the electron microscopic view serves as a useful confirmation that the cells are Sezary cells.

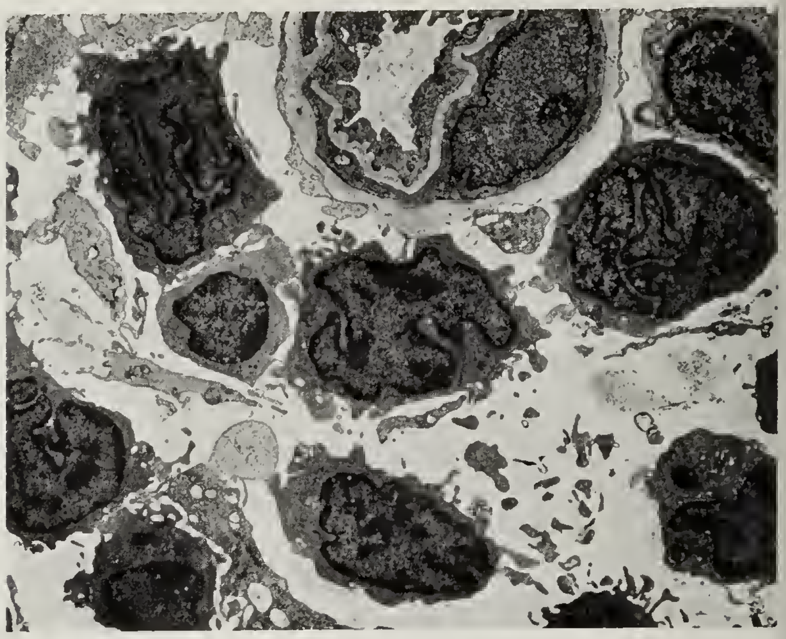


Figure 1
Sezary cell: note cerebriform nucleus

The important question often raised is whether the electron microscope is a useful tool in the early diagnosis of mycosis fungoides before it is identifiable by conventional light microscopy. It should be noted that classical mycosis fungoides is a three stage disease, evolving from its non-specific dermatitis or premycotic stage (which may last many years) into an infiltrated plaque stage and eventually a tumor stage. Despite the variable and often prolonged course of the initial stage, the average survival after a specific microscopic diagnosis can be reached (which is in the 2nd or 3rd stage) is dismal, less than 7 years.[3, 4, 5] Therefore, early detection of mycosis fungoides, in its premycotic stage, may represent an important therapeutic intervention point, with the potential for imporved prognosis.

Unfortunately, the Sezary or mycosis cell is morphologically indistinquishable from normal activated T-cells. It has been recognized by electron microscopy in a number of common benign dermatoses, including allergic contact dermatitis, dermatophytosis, lichen planus, and psoriasis.[6] Thus, one must avoid making the diagnosis of mycosis fungoides solely on the

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From: Univ. of Arizona Health Sciences Center, Tucson, AZ 84724. Dr. Schwartz, Section of Dermatology, Dept. of Internal Medicine, and Dr. Bangert, Dept. of Pathology. Reprint requests to Dr. Schwartz.

electron micrscopic findings of these cells.

It has been mentioned that Sezary cells are probably dentical with the tissue infiltrating cells of classical mycosis fungoides. This concept, although generally accepted, is still debated.[7] Some feel that even morphologically the mycosis cell and the Sezary cell are different, with the latter being slightly more lobulated.[8]

These basic considerations of the Sezary or mycosis cell have become even more complex by the dentification in 1972 of a small cell variant, which is 8 rather than 15-20 microns in diameter. It is difficult to distinguish from the small lymphocyte with routine ight microscopy, although it has a slightly more grooved nuclear pattern. Electron microscopy shows it to be rregular in nuclear outline, but to usually lack the cerebriform pattern characteristic of the usual (large cell type) mycosis or Sezary cell. Both small and large Sezary cells are seen in the same patient, but one type usually predominates.[9] In one series of patients with the Sezary syndrome, 9 of 12 had a predominance of small type Sezary cells.[10] Thus, the electron microscopic examination is very important if one is considering the possibility of circulating small Sezary cells.

It should be pointed out that Sezary in 1949 described four patients with a typical erythroderma who also had cutaneous lesions with the histopathological characteristics of mycosis fungoides including Pautrier microabcesses as well as "cellules monstreuses"—monster cells—in the peripheral blood.[11] He felt that these circulating atypical cells distinguished the process from mycosis fungoides, and considered it "a new cutaneous reticulosis," which he felt was a separate form of lymphoma. Noteworthy is the point that an erythroderma with circulating activated T-cells (which are morphologically identical with Sezary cells) does not provide the diagnosis of Sezary syndrome, the *sine qua non* of which is the presence of a plaque or tumor microscopically diagnostic of mycosis fungoides or another lymphoma. Interestingly, a study of patients with an erythroderma and circulating Sezary cells showed only 14% of them developed a lymphoma, which is less than expected in comparison with patients who have an erythroderma alone.[12] Studies have shown that 17% to 25% of patients with erythroderma alone developed a lymphoma, the erythroderma preceding, following or occurring together with the recognition of the lymphoma.[13, 14] Thus, the value of searching for small Sezary cells may be doubted, although certainly future studies may show their presence or more likely their presence in large numbers to be of prognostic and/or therapeutic value.

There is already evidence that the presence of circulating mycosis cells is of prognostic value in mycosis fungoides. One recent study showed 31% of MF patients without circulating mycosis cells had progressive MF, in comparison to 77% when these cells were consistently observed.[15] Accordingly, a determination of the leukemic stage of MF, the Sezary syndrome, may be an important part of the staging of the lymphoma.

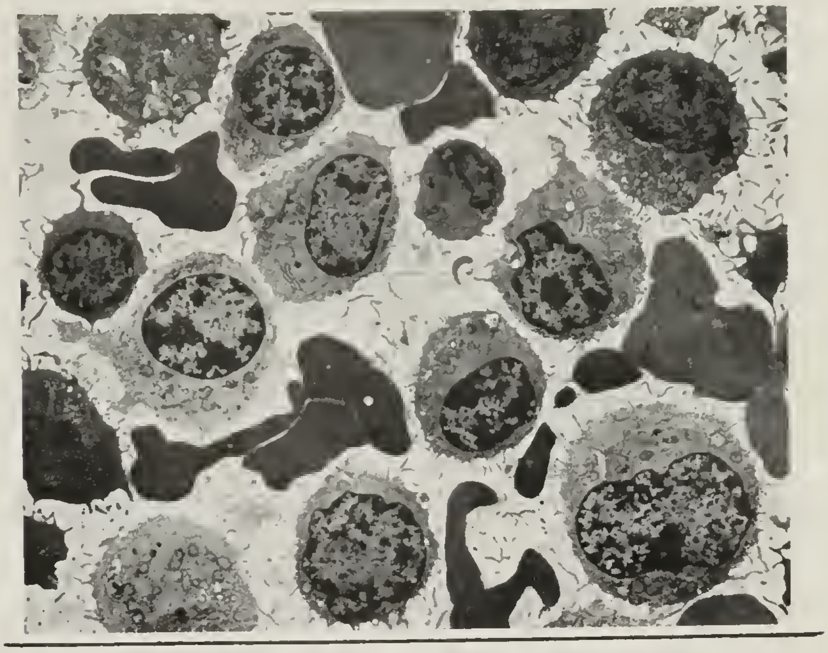

Figure 2
Hairy leukemic cell: note hairy irregular cytoplasmic extensions.

Hairy Cell Leukemia

Histologically specific cutaneous lesions are said to occur in 20% of non Hodgkin's lymphomas, being the pesenting sign in 5% of 1269 patients in one study.[16] Microscopically diagnostic cutaneous or subcutaneous nodules may also occur in a variety of leukemias, sometimes even preceding leukocytosis or overt blood involvement.[17, 18, 19] Hairy cell leukemia (leukemic reticuloendotheliosis) may also show histologically specific cutaneous lesions.[20]

Hairy cell leukemia, also know as leukemic reticuloendotheliosis, is a recently emphasized disorder characterized by hypersplenism, pancytopenia, minimal lymphadenopathy and circulating as well as bone marrow mononuclear cells with irregular hairy cytoplasmic projections. In one series of 18 patients with this disorder, 33% had petechiae and ecchymoses and 17% had maculopapular lesions.[21] In the classical description of this leukemia by Bournocle and associates in 1958,[22] infiltrative but apparently unbiopsied skin lesions were observed in 3 of 26 patients. Biopsied recurrent maculopapules have shown hairy cells both by light and electron microscopy.[23, 24]

However, like the Sezary or mycosis cell in mycosis fungoides, the hairy cell itself does not absolutely confirm the diagnosis of hairy cell leukemia, since it can be found in lymphocytic lymphoma and other leukemia cells.[24] It should be noted that these non-specific hairy cells not only have long microvilli, but in addition have the characteristic ribosome-lamellar complexes (Fig. 2). In addition, the characteristic long microvilli by themselves may be seen in improperly fixed lymphocytes. Ribosome-lamellar complexes by themselves are seen in other hematologic malignancies, such as monoblastic leukemia, Waldenstom's macroglobulinemia and chronic lymphocytic leukemia.[25] Thus, Neiman and associates warn that the diagnosis of

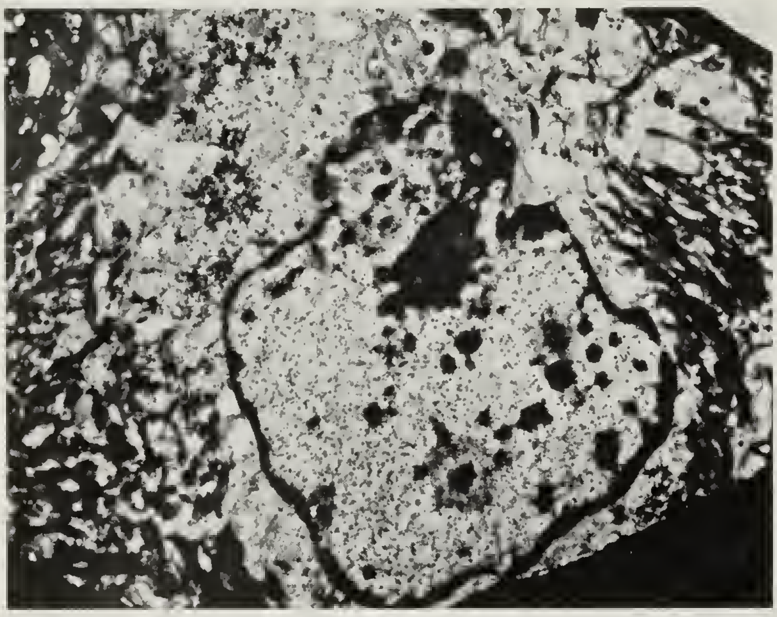

Figure 3
Wart virus particles: these intranuclear DNA virsus each appear round and stippled.

hairy cell leukemia must be made carefully, since lymphocytic lymphomas may be confused with it.

Epidermodysplasia Verruciformis and possible Viral Co-Carcinogenesis

Epidermodysplasia verruciformis (EV) is a rare, frequently familial disorder which is characterized by lifelong, often generalized flat warts, usually first manifest in infancy or childhood. Some have suggested it is an autosomal recessive disease,[26] though this remains to be proven. Electron microscopic studies have revealed the presence of intranuclear viral particles, morphologically similar to the common human wart virus.[27] In addition to the nearly universal presence of flat warts in EV patients, approximately 3/4 will also display pityriasis - like warts.[26] Similar virus particles have been demonstrated in these lesions.[26]

Perhaps the most remarkable characteristic of EV patients is the development of cutaneous neoplasms at an early age. The neoplasms are of either the Bowenoid in-situ type or invasive squamous cell carcinoma and may occur as early as age 13. The mean age for development of carcinoma is 31. From 1/4[28] to 1/3[26] of patients will develop neoplasms. The vast majority of neoplasms arise on sun exposed skin, especially the face, though other sites are occasionally involved.[26] The neoplasms behave as their usual counterparts in non-EV patients.

EV then would seem an excellent model for the study of human viral carcinogenesis or co-carcinogenesis. While the viral particles have been easily demonstrated in the benign lesions of EV, they are nearly always absent in the malignant lesions. Recently, viral particles have been described in a Bowens-type lesion and in an invasive squamous cell carcinoma in a single patient.[29] The number of particles was less than that usually seen in benign lesions. This recently described finding of viral particles in a malignantly transformed lesion awaits confirmation by others.

It has recently been shown that there are at least four types of viruses associated with human warts[28] (Fig. 3). Human papillomavirus, type I (HPV-I) is associated with plantar warts, HPV-2 with common warts, HPV-3 with flat warts, and HPV-4 with pityriasis-like warts. While morphologically similar, these viruses show little or no DNA sequence homology and no antigenic cross-reaction.[28] Orth et al studied 11 patients with EV. None of the lesions studied harbored either HPV-1 or HPV-2.[28] The malignant transformation of some EV lesions into cutaneous carcinoma was more frequently associated with HPV-4 than HPV-3. Four of five patients who developed carcinoma had HPV-4. One had only HPV-3 and another had both HPV-3 and HPV-4. HPV-4 was not isolated in any of the patients who did not develop carcinoma. An important unanswered question is whether HPV-4 or HPV-3 might be the etiologic agent in common viral warts which are reported to have undergone malignant transformation.

Verrucous lesions on the genitalia of young people are usually condylomata acuminata. However, a few will histologically be Bowen's disease.[30] Reports of carcinoma-in-situ in virus containing lesions, which were clinically condylomata acuminata[31,32] suggest another disease in which possible viral carcinogenesis may be important.

A close relative of the HPV's is the polyoma (Py) virus, capable of inducing sarcomas in certain animal models. Meyer has proposed the Py virus as a simple model for transformation by a DNA virus to be used as a model for viral skin carcinogenesis.[33] This would seem a reasonable approach to the problem of cutaneous viral carcinogenesis, since genetic factors and environmental factors (e.g. ultraviolet light exposure) might be controlled. The role of the virus in cutaneous carcinogenesis might then more easily be identified.

An Overview

The electron microscope is a valuable research tool which is being employed as another parameter by which to view many disease processes cutaneous and noncutaneous. Accordingly, a high number of clinical and research publications employ this technique, often in an attempt to understand the pathogenesis of each process. In many cases the results are rather interesting, although of unknown significance. For example, giant melanosomes have been demonstrated in a large number of disorders, including nevus spilus, melanocytic nevi, the multiple lentigines syndrome, xeroderma pigmentosum, cafe-au-lait spots of neurofibromatosis, the melanotic macules of Albright's syndrome, the depigmented regions around cutaneous melanoma, in both the eye and skin of patients with X-linked ocular albinism, and even in the skin of normal individuals.[34] Accordingly, what was thought to be a specific finding in the autosomal condition of von Recklinghausen's neurofibromatosis (which has a significant incidence of neurofibrosarcomas, Wilm's umor and certain childhood leukemias[2]) is not so pecific after all.

However, as more and more electron microscopy is one, disease categories will undoubtedly be identified y this tool. Although its use is limited in epidermal skin ancers in terms of our present knowledge at least, good tudies in cutaneous sarcomas may be more fruitful. his is especially true with regard to the so-called nalignant fibrous histiocytoma and the atypical ibroxanthoma.[35] In fact, Barr and his associates uggest that the light microscopic diagnosis of atypical ibroxanthoma represents a number of different eoplasms and strongly urge further electron nicroscopic study of patients with this diagnosis.

Another example of the use of electron microscopy is llustrated in a patient with cutaneous leiomyosarcoma n whom its use confirmed the diagnosis by lemonstrating the ultrastructural characteristics of mooth muscle cells.[36] Still another example of the use f EM is a recent ultrastructural study of trabecular arcinoma of the skin. This uncommon malignancy, reviously classified as probably of epidermal sweat land origin, has been recently shown to be composed of ells resembling Merkel cells[37] and may thus be a nalignant trichodiscoma, which would be a nerve tissue arcoma. Thus, the use of EM for the diagnosis and lassification of cutaneous tumors can be of real clinical alue.

The use of EM in cutaneous lymphomas has already een discussed with regard to mycosis fungoides and airy cell leukemia. Recent evidence suggests that it may lso be helpful in patients with immunoblastic arcoma.[38] This disorder commonly displays cutaneous esions which may have specific cutaneous histology.[2] The finding of tennis racquet-like intracytoplasmic ranules in the cutaneous and extracutaneous lesions of ll three types of histocytosis X (which may be onsidered a type of histiocytic lymphoma) is interesting ut usually only of confirmatory diagnostic value, The urrent re-analysis and reclassification of the ymphomas appears to be profiting from electron microscopic study used in combination with other vailable techniques.

Cutaneous metastatic disease represents another ategory in which electron microscopic characteristics may be of clinical value. Cutaneous metastases occur in 4.4% of patients with visceral cancer,[39] often hematogenously as an early event. Surprisingly, when they occurred, they did so before the underlying malignancy was diagnosed in 60% of patients with lung cancer, 53% of patients with renal cancer, and 40% of patients with ovarian cancer.[40] However, most cutaneous metastases are either adenoid, squamous, or anaplastic, although a few types of cancer have specific cutaneous histology. The latter group includes follicular thyroid carcionoma, malignant carcinoid, melanoma, hepatoma, testicular seminoma, hypernephroma, and fetal testicular choriocarcinoma. In anaplastic metastatic disease when a question of possibly specific histology is considered, an electron microscopy view may provide important clues for the detection and therapy of early visceral malignancies. The question most ofen appears in the consideration of the diagnosis of melanoma in tumor sections whcih appear rather undifferentiated. The recognition of hypernephroma and placental choriocarcinoma are especially important, since both may be cured even with metastatic disease.[2]

Thus, the use of electron microscopy in cutaneous oncology provides a potentially useful tool for investigation when properly correlated with the gross pathologic findings (the skin lesion) and the light microscopic findings.

Acknowledgement

The authors wish to thank Ray B. Nagle, M.D. and Claire M. Payne, Ph.D. for use of electron microscopic materials.

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Balance of References available upon request.

Current Status of Surgical Procedures for Morbid Obesity

Hugo V. Villar, M.D.

Morbid obesity, defined as body weight twice the expected, is a significant problem in the U.S.A. The Framingham studies [1] have documented increased risk of sudden death and increased chances of coronary occlusion. In addition, the individual with morbid obesity will develop diabètes, renal disease and coronary artery disease at a higher rate than ordinary individuals.[2,3] Varying methods have been used to treat severe exogenous obesity. Psychiatric counseling, though successful in some instances, has been a failure due to the inability of the psychiatrist to change the patient's image of himself. Supervised fasting has been attempted repeatedly in the treatment of morbid obesity.[4] Prolonged hospitalization will achieve weight loss, however, most patients regain their weight after release from hospital confinement. After one year, fully 80% of those observed had either equalled or exceeded their pre-fast weight. In addition, Drenick[5] has called attention to the unfavorable side effects of prolonged fasting, especially severe depression, suicidal tendencies and other frank psychoses.

Surgery has been involved in the treatment of severe obesity for about 20 years. In 1954, Kremen et al[6] performed the first jejunoileal bypass for morbid obesity. Payne et al[7] in 1963 first reported 10 patients in whom a jejunocolic shunt was performed. They divided the bowel 18 inches from the ligament of Trietz and anastomosed the jejunum to the transverse colon. Uncontrollable diarrhea and electrolyte problems forced them to dismantle these bypasses. The anastomosis to the transverse colon was moved to the distal ileum. End-to-side jejunoileal bypass, Payne's procedure, has become the most successful surgical treatment of morbid obesity. It is estimated that about 10,000 jejunoileal bypasses have been performed in this country. Because some patients did not lose weight at a satisfactory rate, or they plateau too early, Scott et al modified the bypass. They converted the end-to-side anastomosis to and end-to-end jejunoileostomy in order to prevent reflux in the excluded loop and minimized reabsorption. (Fig. 1) Small intestinal bypass controls morbid obesity by reducing absorption of carbohydrates, proteins and fats. Food intake is not limited except for those patients who develop anorexia if they become ill from diarrhea. Weight loss is effected by rapid transit of ingested materials through the shortened small bowel, resulting in diarrhea. In essence, a controlled malabsorption is created. Weight loss is approximately 8 to 10 pounds per month during the first year, 4 to 6 pounds during the second year, and usual plateau at the third year. About 50% of patients wh underwent jejunoileal bypass will have a satisfactor weight loss. Side effects and complications of jejunoile bypass include uncontrollable diarrhea and electroly imbalance, protein malnutrition, iron deficiency anemi liver failure and cirrhosis. Increased reabsorption oxalate may occur and may lead to an increased inciden of kidney stones. A migratory form of polyarthralgi most likely secondary to reabsorption of an E-co antigen from the excluded loop, has also been reporte Postoperative management after jejunoileal bypas includes a high protein low fat diet, and electrolyte an vitamin replacement. Potassium, magnesium an calcium must be replaced from the time of discharg Magnesium and calcium will, in addition, prevent th excessive reabsorption of oxalate and minimize th formation of kidney stones. Overall satisfaction wit jejunoileal bypass is, in general, excellent. About 15% patients will fail to lose weight or will plateau too earl This is secondary to elongation and hypertrophy of th small intestinal mucosa. Revision of the jejunoile bypass and shortening of the loop is possible wit satisfactory results. Some problems with the exclude loop, intussusception, bypass enteritis, and small bow obstruction are also possible.

In summary, jejunoileal bypass, either end-to-side o end-to-end achieves, in the majority of cases, it objective, i.e. patients do lose weight at a satisfactor rate. Careful follow up with attention to a high protein low fat diet and electrolyte replacement are essential complications are to be minimized. Liver failure is dreadful and serious complication that may occur an time after jejunoileal bypass.

In 1967, Mason[8] described his experience with gastri bypass and gastroplasty. His operation was based on th observation that extensive gastric resection with Bilroth II anastomosis will produce weight loss almos routinely. His initial operation was basically 90% gastri exclusion with continuity re-established through retrocolic gastroenterostomy. A modification of thi operation was called gastroplasty. This operatio consisted of dividing the stomach into 2 pouches, leavin a small shunt by the lesser curvature for emptying. (Fig 2) Weight loss was much more satisfactory with th gastric bypass and the gastroplasty was abandoned Alden's[9] modification of Mason's technique ha significantly reduced the risk of upper pouch necrosis He simply stapled the stomach across with the TA-9 automatic stapler without dividing the stomach. A smal gastroenterostomy (12 mm) was constructed on th anterior surface of the upper pouch. Since the firs gastric bypass was performed by Dr. Mason on May 10 1966 he has reported over 600 patients.[10,11,12] Gastri bypass is now considered an effective and saf alternative to intestinal bypass for the treatment o mobidly obese subjects who have failed non-operativ treatment. Gastric bypass provides weight loss b

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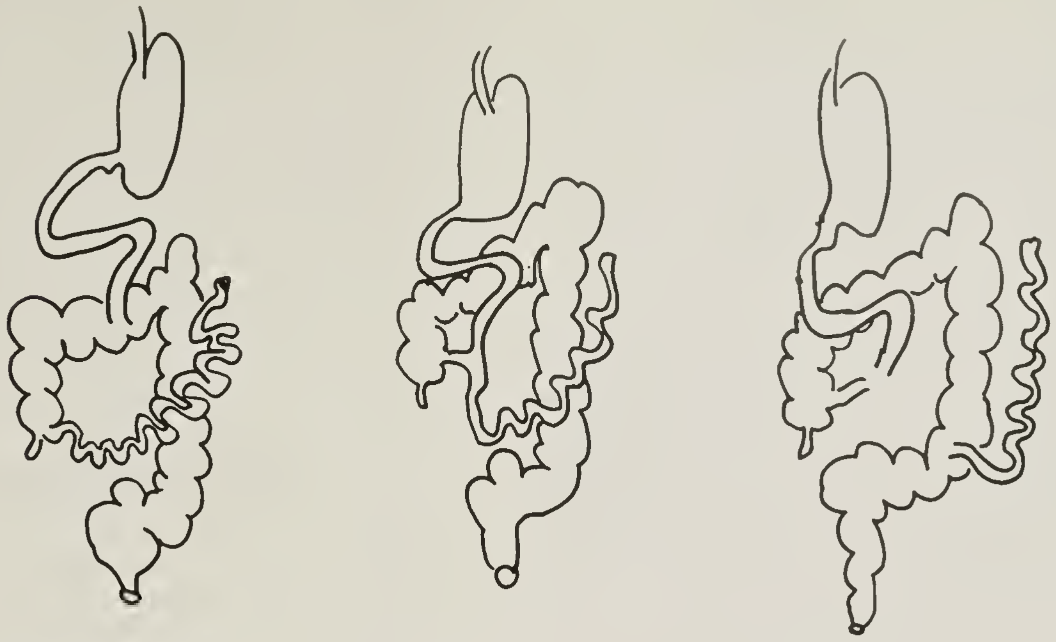
From: Univ. of Arizona Health Sciences Center, Dept. of Surgery, Tucson AZ 85724. Dr. Villar Assoc. Professor of Surgery.

FIGURE 1.

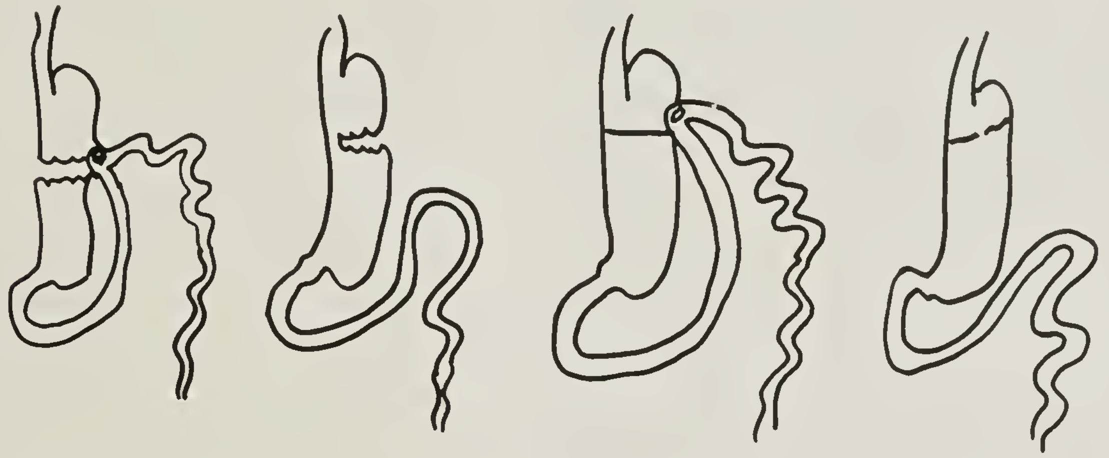


Jejunocolic Shunt

End-To-Side Jejunoileostomy (Payne's)

End-To-End (Scott's)

FIGURE 2.



Gastric Bypass (Mason's)

Gastroplasty

Alden's Modification

Gastric Stapling

providing a functional gastric capacity of less than 100 ml and consequently forces reduction of food intake. The main criticism of the gastric bypass is the creating of a large blind area in the stomach and duodenum. Gastric bypass is basically an antral exclusion in which antral neutralization depends on the amount of parietal cell mass left in continuity with the antrum in the distal pouch. If the amount of parietal cell mass left in the distal pouch is not enough, or does not produce enough acid, it is reasonable to expect a large number of stomach ulcers from continuous antral stimulation without the inhibition of gastrin release provided by the production of acid. The reported incidence of marginal ulcer is about 2% in Mason's series. In addition to the problem of stomal or duodenal ulceration, gastric bypass makes the area completely inaccessible for further diagnosis and investigation. In the event that antral carcinoma or duodenal ulcer develop, the diagnosis will be delayed.

Three prospective studies have been done in order to compare the effectiveness, mortality and morbidity of gastric and jejunoileal bypass for the control of morbid obesity.[13, 14, 15] Gastric bypass operation was associated with a slightly higher early complication rate, indicating that this is a more technically demanding procedure. The main difference was that the late sequelae were more prominent in the jejunoileal bypass. Significant diarrhea occurred in over 50% of the patients, requiring replacement medication, mostly electrolytes and vitamins. The appearance of oxalate renal stones and cholelithiasis also complicated the jejunoileal bypass and was not seen after gastric bypass. In Griffin's series there were 2 late deaths, one in each group. Weight loss, the main aim of the operation, was similar with both operations.

Modification of gastric bypass, gastric stapling, is becoming increasingly popular. (Fig. 2) In this operation, the stomach is divided into 2 pouches, an upper fundic pouch with a capacity of 100-150 ml is created by

Table 1

	Number of Patients	Deaths	Failure to Lose Weight	G.I. Bleeding
Jejunoileal Bypass	10	0	2	0
Gastric Bypass	16	1	2	2
Gastric Stapling	36	0	2	0

stapling the stomach across with a TA-90 stapler. Three staples from the center of the cartridge are removed prior to its use. An 8 mm opening communicated the upper and distal pouches. Differing from the early gastroplasty described by Mason, the opening has less surface area that could dilate or stretch. Continuity of the stomach is maintained. Food is allowed to flow slowly from the upper pouch into the distal stomach. The ability of food to buffer the antrum is retained and therefore these patients should be better protected against the development of duodenal ulcer in the excluded stomach.

Since January 1977 sixty two patients have undergone surgical procedures for the treatment of morbid obesity at the Arizona Health Sciences Center. (Table l) Ten patients underwent an end-to-side jejunoileal bypass, 16 patients a gastric bypass, and 36 a gastric stapling. Another 5 patients have been referred to us for complications of the jejunoileal bypass, 2 have been dismantled completely restoring normal anatomy and 3 underwent gastric stapling at the time of dismantling.

The results with the jejunoileal bypass group were as follows. There were no deaths or major surgical complications. Two patients have failed to lose weight or they have plateaued too early. One of these patients had had her bypass shortened. The initial 14 and 4 inches of jejunoileum had elongated to 28 and 6 inches. One patient had her bypass dismantled because of uncontrollable diarrhea and rising bilirubin. The other 7 patients have lost weight at a satisfactory rate and have had not major complications. Patient staisfaction has been excellent. The group of 16 patients with gastric bypass includes one death on the 40th postoperative day. No satisfactory explanation for her death was found at the necropsy. Two patients had failed to lose weight at a satisfactory rate and they had plateaued after losing 50 and 60 pounds respectively. Two patients at 3 and 12 months after their bypasses have been re-admitted with massive melena and hematemesis. Both have had spectacular weight loss. No marginal ulcers were present. Most likely they were both bleeding from duodenal ulcers. The bleeding has recurred 3 months later on one patient after ingestion of Butazolidin. Both patients are currently on cimetidine.

Weight loss in the gastric stapling group has been excellent averaging 16 pounds in the first month and 10 pounds thereafter. There have been no operative deaths or complications in this group. Two patients have failed to lose weight. The longer follow up on this group is months. Average hospital stay after gastric stapling is days.

Gastric stapling is, in our opinion, a safe, simple ar effective way of dealing with the problem of morb obesity. A feeling of fullness is the only side effect. It i in our opinion, a definite advantage over the Masc gastric bypass. Longer follow up is needed to determir if the long term result of gastric stapling will be spectacular as jejunoileal bypass. Its simplicity ar carefree postoperative period make it, at the preser time, an almost ideal solution for the morbid obesit patient. We believe that surgical intervention for th control of morbid obesity should be reserved to larg centers where facilities and interest for the follow up these patients are present. The numerous anatomic variations of either jejunoileal, gastric bypass or gastr stapling make mandatory that the individuals takin care of these patients be quite familiar with thes procedures.

Who is a candidate for a bypass or gastric stapling? W believe the patient should be at least 100 pound overweight or at least 2-3 times the ideal weight befor consideration for the operation. The mean preoperativ weight in our patients was 290 pounds and the mea height was 5′2″.

Summary: jejunoileal and gastric bypass are accepte surgical options to treat morbid obesity. Gastric staplin seems a safer and a simple operation devoid of th complications of both jejunoileal and gastric bypass Careful follow up is essential to evaluate the long tern benefit of any of these interventions.

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Malignant Hyperthermia

Thomas J. J. Blanck, M.D., Ph.D.
Raphael Gruener, Ph.D.
William J. Casey, M.D.
Lawrence Z. Stern, M.D.

Unexplained tachycardia, muscle rigidity, and fever are ominous signs in the anesthetized patient. Any one of these signs might be the initial manifestation of a deadly syndrome, malignant hyperthermia. This lethal syndrome is triggered by anesthetics. Almost every anesthetic, in particular halothane, has been implicated as the inciting drug. The mechanism by which this occurs is unknown. The patients who are at risk of developing this disorder are also unidentified.

The purpose of this paper is to describe briefly the syndrome of malignant hyperthermia and inform the readers of the availability of diagnostic studies for patients susceptible to this syndrome at the Arizona Health Sciences Center.

A letter was published in the *Lancet* in 1960, describing the anesthetic-caused death of 10 patients from the same family.[1] These tragic deaths were all marked by severe increases in body temperature. The appearance of this letter signified the initial awareness of a syndrome whose hallmarks were hyperthermia, muscle rigidity, and sudden death. Since that time there have been numerous reports of rapid temperature elevations occuring after induction of anesthesia.[2,3] Most anesthetics have been implicated including halothane, ketamine, and ether; the muscle relaxant succinylcholine is also known to initiate malignant hyperthermia in certain individuals.[4]

One of the first manifestations of this syndrome is tachycardia.[5] The usual causes of tachycardia during anesthesia must be ruled out, e.g. light anesthesia, excessive blood loss, and pharmacologically induced tachycardia. If there is no obvious cause for the tachycardia the anesthetist must suspect malignant hyperthermia. The susceptible patient may have demonstrated excessive faciculations or prolonged rigidity after succinylcholine administration. However, not all patients with malignant hyperthermia experience muscle rigidity.[6] A late and ominous sign of this syndrome is an elevated temperature. Twenty minutes or more after the induction of anesthesia the patient might feel hot. Temperature elevations to 110° F have been observed in this short time span.[2] Elevation of temperature to this degree can of itself lead to severe cardiac arrhythmias. Several metabolic problems arise while this disastrous sequence of fever and rigidity ensues. Muscle tissue is breaking down which results in an increase in serum K^+; CO_2 production is markedly increased leading to acidosis.[7] The increased temperature compounds the problems of hyperkalemia leading to cardiac arrhythmias and ultimate cardiovascular collapse. In the unusual instance when the initial crisis is past, problems of renal failure and coagulopathies may develop. The only certainties in the treatment of this disorder is that the anesthetics should be turned off and all efforts directed toward cooling the patient and limiting the cardiac arrhythmias.

Fortunately this is a rare syndrome, occuring in 1 in 50,000 adults and l in 15,000 children. Unfortunately the mortality rate approaches 70%. Since there are at least 25,000,000 anesthetics given in the U.S. each year between 500 and 1,000 patients suffer from this syndrome and between 350 and 700 patients die from this syndrome each year.

At present we do not know which patients are at risk of developing malignant hyperthermia. It is stated that patients with clinically evident muscle disease may have a higher incidence of this syndrome than the normal population.[6,8] The only other leads to go on in avoiding

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From: Univ. of Arizona Health Sciences Center, Tucson AZ 85724. Dr. Blanck, Dept. of Anesthesiology; Dr. Gruener, Dept. of Physiology; Dr. Casey, Dept. of Surgery; and Dr. Stern, Dept. of Neurology.

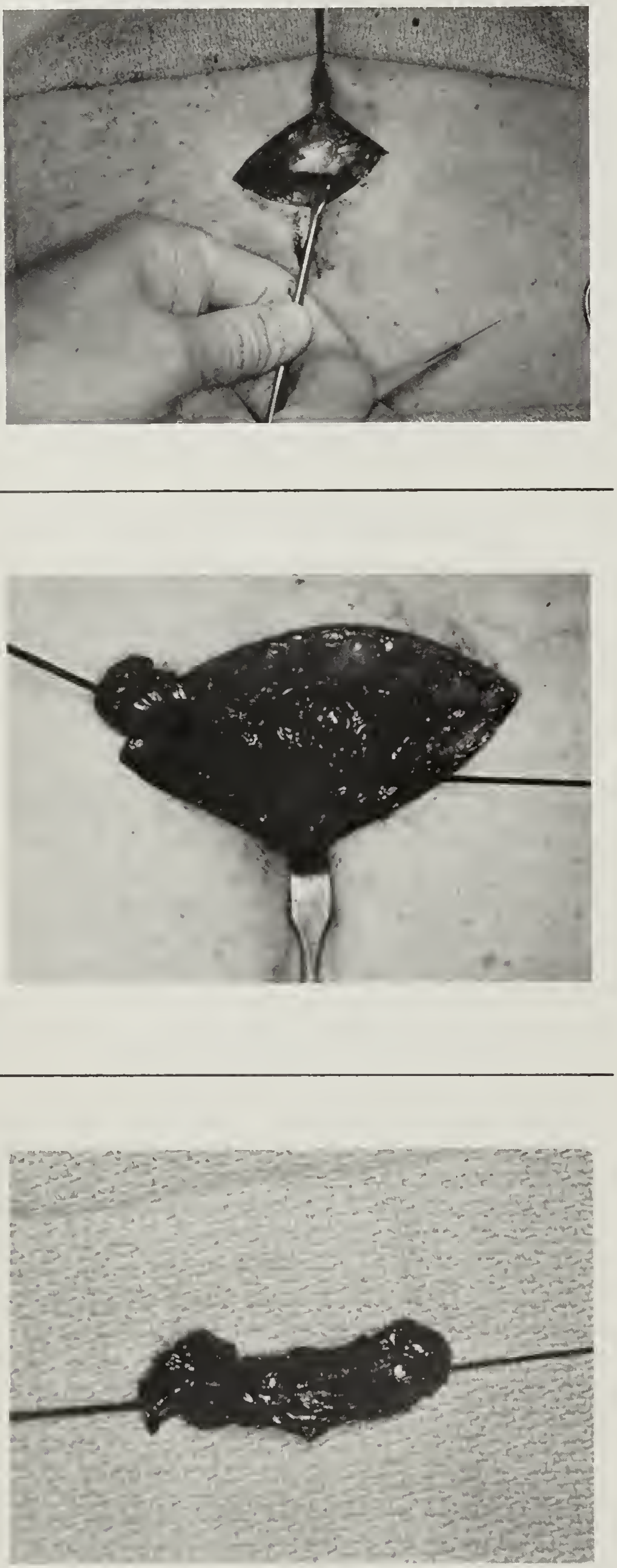

Figure 1 a,b,&c
The incision and exposure of the vastus lateralis are demonstrate in 1-a. Excision of the muscle is shown in 1-b. The excised muscle used for physiologic measurements is 1.5 inches long and 0.5 inches wide (1-c).

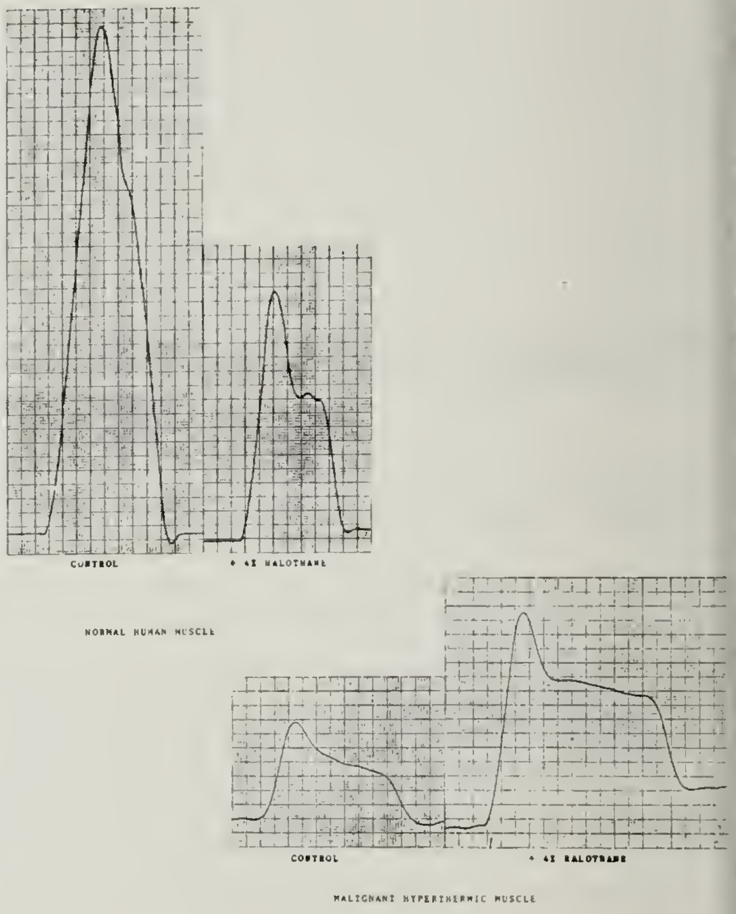

Figure 2
The effect of halothane on development of tetanic tension by norm muscle is shown in the upper graphs. The lower graphs demonstra the response of malignant hyperthermic muscle.

this type of reaction is a thorough family histor pointedly asking if any other members of the famil have had difficulties with anesthesia.

The pathophysiology of this syndrome is uncertair There is strong evidence that it is a muscle disease an that the anesthetics unmask an abnormality in th movement of calcium in the muscle cell. The mechanisn by which this leads to the tremendous production o heat is not fully explained.

At the Arizona Health Sciences Center we hav undertaken a study into the biochemical and physiologi abnormalities of malignant hyperthermic muscle. Thi research is supported by the Muscular Dystroph Association of America. The immediate clinical result o this research project is that we now have the capabilit of diagnosing malignant hyperthermia in biopsie muscle. Muscle biopsies are performed on patients o family members suspected of having the disorder. Th biopsies are done on an outpatient basis and they are al performed in the operating room in the event that malignant hyperthermic reaction might occur.

The patient is brought to the OR withou premedicaiton. An intravenous line is begun and th temperature, cardiac rhythm and blood pressure ar monitored. Thus far we have used no intravenous or inhalational sedation, however, an anesthesia machine which has been purged of halothane for 24 hours is available in the room if O_2 administration or O_2-N_2O administration are deemed necessary. One percent lidocaine infiltration is used for anesthesia. The muscle biopsy is taken from the vastus lateralis. Figure 1, a,b,c, demonstrate the biopsy procedure. A total of approximately 2.5 gm of muscle are removed for diagnostic, physiologic, biochemical, and histologic examination. The piece of muscle used for diagnosing susceptibility to the syndrome is kept in oxygenated balanced salt solution and is immediately taken to the laboratory of Dr. Raphael Gruener in the Department of Physiology. He dissects the muscle into several muscle strips each containing about 50-100 fibers. The strips are kept in cold oxygenated saline solution until they are used. Each strip is mounted into a temperature controlled chamber and connected to a transducer which measures the tension that the muscle generates. The muscle is then exposed to halothane and its response recorded. Figure 2 shows the difference in response to halothane of normal muscle and muscle from susceptible patients. The tetanic tension of control muscle is depressed by halothane while malignant hyperthermic muscle contracts with greater force. This is the major laboratory criterion used for determining a patient's susceptibility to malignant hyperthermia. Because of the relative newness of these types of studies it is as yet uncertain whether all of the patients who demonstrate this type of response would truly develop malignant hyperthermia and, conversely, whether there are some patients who would develop malignant hyperthermia whose muscle would not respond to halothane in the way described.

Currently we are recommending to the patients whose muscle responds positively to halothane that they warn their physicians that they have malignant hyperthermia and carry a medical alert bracelet indicating that they suffer from malignant hyperthermia.

Further investigations into this disorder requiring the study of more biopsy muscle from patients who have had a malignant hypertermic response will enable us to refine our diagnostic studies and make them available to the general operating room population.

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Percutaneous Transluminal Coronary Angioplasty: Can Cardiac Catheterization Be Therapeutic?

Lawrence P. Temkin, M.D.

The treatment of symptoms and improvement of prognosis of patients with obstructive atherosclerotic coronary artery disease has formed a major focus for the research efforts of cardiologists and cardiovascular surgeons for the past 20 years. The availability of coronary arteriography has allowed accurate diagnostic delineation and assessment of the severity of obstructive lesions. Pharmacologic therapy has been directed toward improvement of the symptoms of angina pectoris with no demonstrated means available for the amelioration of the severity of obstructive lesions. The advent of coronary artery bypass surgery has met with widespread success as a palliative therapeutic maneuver. Surgical intervention, however, remains associated with a small but significant associated risk of mortality and morbidity.

A search for alternative methods for the treatment of coronary artery disease has spawned several technological innovations. The most recent technique advocated as a potential "non-operative" approach to obstructive disease has been termed "percutaneous transluminal coronary angioplasty" by its developer, Dr. Andreas Gruntzig.[1] The technique is based on the concept that the morphology of a coronary artery atherosclerotic lesion may be altered by local compression in such a way that the residual lumen dimension at the site of narrowing might be favorably increased. Such "dilatation" would either compress the lesion to the arterial wall or, in some way, alter its geometry to allow an expanded transluminal orifice.

A diagram of the catheter designed to perform such dilation is shown in Figure 1. The catheter is approximately 1 mm in diameter and has a small flexible guide wire at its tip. It consists of two internal lumens. One lumen is hollow and permits pressure to be recorded from the two side holes located at the catheter

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From: Univ. of Arizona Health Sciences Center, Sect. of Cardiology, Dept. of Internal Medicine, Tucson, AZ 85724. Dr. Temkin, Assist. Professor of Medicine, and Director, Cardiac Catheterization Laboratory.

tip and allows dye material to be injected. The second lumen controls the inflation of an oblong balloon located at the distal end of the catheter, proximal to the pressure lumen side holes. The maximal inflated diameter of the balloon is approximately 3mm. The dilatation catheter, therefore, allows both pressure monitoring and balloon inflation capabilities.

The procedure for percutaneous transluminal angioplasty involves a two-catheter system. As shown in Figure 2, a guide catheter is placed fluoroscopically in the orifice of the affected coronary artery utilizing a percutaneous approach from the femoral artery. When the guide catheter position has been confirmed, the dilatation catheter, previously described, is inserted through the guide catheter and advanced within the lumen of the coronary artery to the level of the lesion while pressure is monitored. With varying degrees of manipulation, the dilatation catheter is then advanced through the orifice of the offending lesion and the catheter position traversing the stenosis documented fluoroscopically. As shown in Figure 3, under constant control, the balloon is inflated using a solution of saline and radio-opaque contrast to a maximal pressure of 5-6 atmospheres for approximately 5-7 seconds. The balloon is then deflated and the degree of dilatation documented angiographically. The procedure may be repeated if initially unsuccessful.

Several technical problems exist in the use of the dilatation device. The guide catheter must be properly shaped to allow selective cannulation of the chosen coronary artery. The dilatation catheter has limited maneuverability within the coronary lumen, thus limiting the control of its placement. As such, selective cannulation of a coronary artery branch, particularly in the case of the left coronary system, may be quite difficult. To some degree, this can be overcome by variation in the shape of the flexible catheter tip guide wire, but appropriate placement remains a significant problem in many cases. The degree of stenosis may be quite substantial, making trans-lesional catheter passage quite difficult. In general, the appropriate use of the device requires a great deal of technical expertise.

It should be noted that all patients undergoing transluminal angioplasty are treated with anticoagulant (Heparin, Warfarin), antiplatelet (low molecular weight Dextran, Dipyridamole), and antispasmodic agents (Nitroglycerin, Nifedipine) to limit local coronary thrombosis and spasm at the site of dilatation. In addition, no procedure is attempted unless preparations have been made for immediate surgical intervention and potential emergent coronary bypass if complications arise during dilatation.

Reported clinical experience with the percutaneous transluminal coronary angioplasty procedure has been quite limited.[1-5] The largest multicenter experience comprises 65 patients.[5] It has been stated that 60% (39/65) of patients having undergone the procedure evidenced improvement as judged by parameters

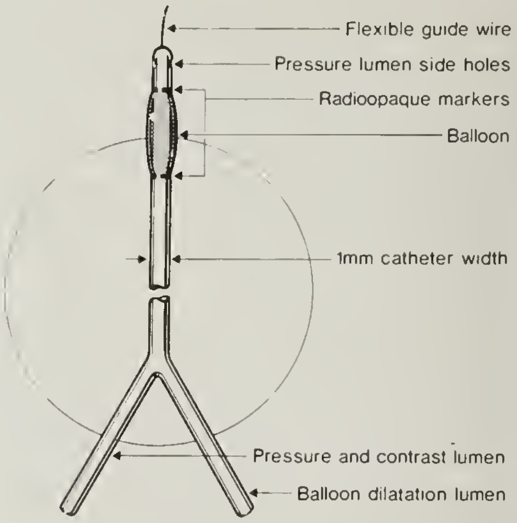

Figure 1
Design of the percutaneous transluminal coronary angiopla dilatation cathether.

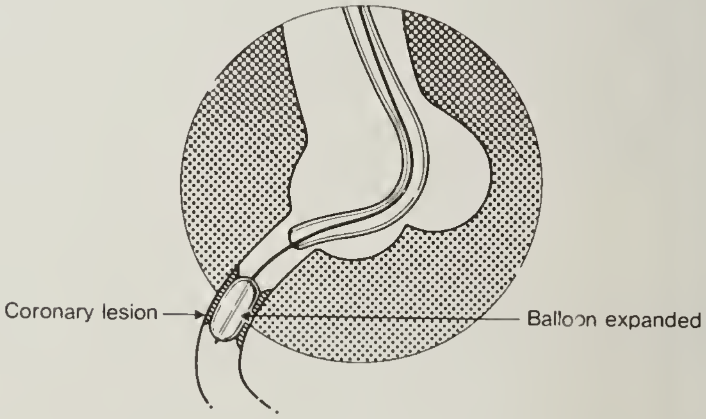

Figure 2
Guide catheter cannulation of coronary artery and trans-lesion placement of dilatation chatheter.

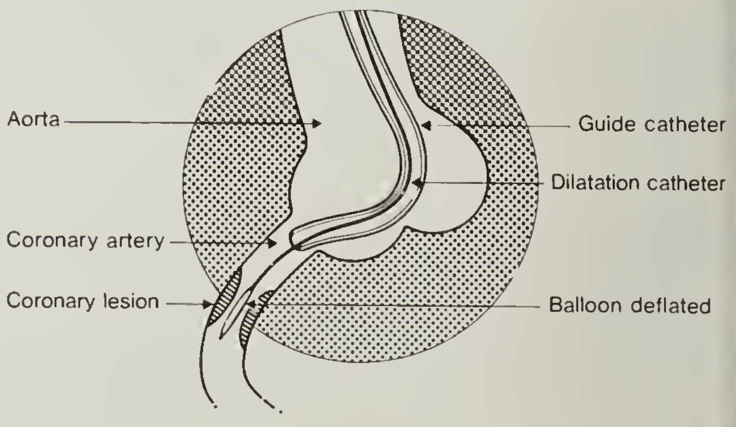

Figure 3
Inflation of the balloon of the dilatation catheter -compression of th coronary lesion.

including post-dilatation angiography, and submaximal work capacity. In a selected population of these patients, improvement in thallium myocardial perfusion image during stress has been demonstrated with sustained improvement shown prospectively at six months in a small group studied.[4] Significant complications have been limited to acute occlusion presumed to be thrombotic at the site of dilatation requiring emergency coronary bypass to be performed in 9.3% of cases (7/65)[5] with one recorded myocardial infarction noted.

In interpreting the results of early experience with the procedure with reference toward potential clinical utility, several points must be raised. The presumed efficacy in patients successfully dilated has been largely based on post-dilatation angiographic appearance and degree of luminal diameter enlargement. To date, the study of the local effects of dilatation on lesion morphology has been limited to the examination of human autopsy specimens[6-9] or animal models.[10-12] In general, it has been shown that transluminal angioplasty is associated with a high incidence of histologic evidence of local injury. Evidence of intimal disruption, plaque rupture, dissection of adjacent normal coronary segment, and perforation have been demonstrated.[7] In addition, electron microscopic examination has indicated post-dilatation denudation of intimal endothelium with superimposed platelet aggregation and mural thrombus formation at the site of expansion.[11-12] It would appear that balloon dilatation is locally traumatic and potentially thrombogenic. This could account for the 9.3% occurrence of acute occlusion necessitating immediate surgical intervention previously noted. Therefore, 'in a substantial number of cases, the dilatation procedure has not only not been palliative, but has precipitated the necessity for emergent surgery presumably on the basis of acute thrombosis secondary to local trauma.

The reports to date have not specifically documented the number of patients submitted for dilatation in whom the procedure could not be technically accomplished for reasons previously cited. It would seem, however, that approximately 40% of attempted cases have been unsuccessful to date[13] emphasizing the technical problems inherent in the technique.

The incidence of additional complications of dilatation as a result of anticoagulation, percutaneous arterial access, transient arrhythmia, occurrence of angina, and myocardial infarction have not been clearly established and the potential morbidity of the procedure has yet to be defined.

In view of these limitations in the small number of patients studied, it is impossible at present to clearly delineate the subset of potential surgical candidates with obstructive coronary artery disease in whom transluminal angioplasty might represent an appropriate alternative to coronary bypass. Initial experience has suggested that calcific lesions are difficult to dilate[3,5 7-9] and that attempted dilatation of distal lesions has been associated with significant local complications[6] and poor patency rates.[3,5] It would seem that the procedure might only be indicated in cases of non-calcific, discrete, subtotal proximal coronary stenoses. This group might represent as few as 10% of all potential bypass surgery candidates. Only future research efforts and expanded technical experience can determine if this small select population might be expanded.

In summary, it seems quite clear on the basis of early studies that the percutaneous transluminal angioplasty technique may offer a potential therapeutic extension to the established diagnostic efficacy of cardiac catheterization in patients with coronary artery diease. To date, multiple potential technical difficulties and potential risks of the procedure have been demonstrated and physicians must be aware that further prospective study must be undertaken to clearly define the potential benefits to appropriately selected patients if the procedure is to be considered an alternative to coronary artery bypass, even in a small population of surgical candidates. Widespread proliferation of laboratories performing the procedure on an uncontrolled clinical basis would seem premature, unwarranted, and ill-advised at this time. Percutaneous transluminal coronary angioplasty must be considered experimental at present and is yet to be established as a viable or appropriate therapeutic alternative for patients with coronary artery disease.

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Immunofluorescence in the Diagnosis and Management of Cutaneous Disease

Norman Levine, M.D.
Raymond B. Nagle, M.D.

The diagnosis of cutaneous disease often requires adjunctive laboratory determinations to help differentiate clinically similar processes. Immunofluorescence has become an important tool in diagnosing and managing a number of cutaneous problems. This paper shall briefly describe fluorescent antibody techniques and their uses in clinical dermatology.

Fluorescence microscopy relies on the fluorescence of certain materials called fluorochromes, which absorb energy in the form of specific wavelengths of light and emit energy at a higher, visible wavelength. The fluorescence microscope is a specially adapted instrument which allows only the appropriate wavelength of light to fall on the fluorochrome, thus producing an intense, uniform fluorescence pattern.

In immunofluorescence, a fluorochrome (usually fluorescein isothiocyanate) is bound to an antibody. When the tagged antibody is incubated with an antigen, an antigen-antibody complex is formed and when observed under the fluorescence microscope, the presence and pattern of antigen-antibody deposition can be determined. To identify autoantibodies (antibodies against self-antigens), anti-human antibodies are produced in animals, conjugated with the fluorescein and incubated with the suspected human antibodies. In this situation, human antibodies become antigens for the fluorescein-labelled antisera.

There are two basic techniques of immunofluorescence used in dermatologic diagnosis. Direct immunofluorescence detects the presence of tissue-fixed antibodies which are usually autoantibodies directed against a constituent of the patient's skin (Fig. 1). Indirect immunofluorescence identifies circulating antibodies in the patient's serum (Fig. 2).

Figure 1 Direct immunofluorescence testing of skin biopsies

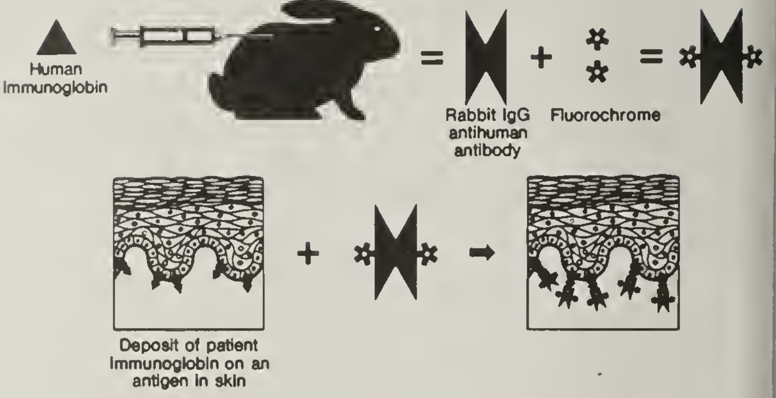
Human Immunoglobin
=
Rabbit IgG antihuman antibody
+
Fluorochrome
=
+
Deposit of patient Immunoglobin on an antigen in skin

Figure 1

The immunologic bullous diseases, pemphigus, bullous pemphigoid, and dermatitis herpetiformis require immunofluorescent studies to confirm the clinical diagnosis. Pemphigus vulgaris is a serious blistering disease usually affecting both the skin and mucous membranes. It may be an acute or chronic disease and has a high mortality if left untreated. These patients usually have IgG and complement fixed to the surface of the keratinocytes of the epidermis. Direct immunofluorescence shows a fish-net-like pattern i involved and uninvolved skin (Fig.3). This pattern quite specific for pemphigus. Some patients with benign variant, pemphigus foliaceous may ha preferential localization of antibodies in the upp epidermis.[1] The exact nature of the epidermal antige is unclear but they appear to be on the surface epidermal cells. These patients also have a circulati antibody which, on indirect immunofluorescence, shown to be directed against the same epiderm antigens identified on direct immunofluorescence. Mo investigators believe that one can follow the course the disease by monitoring the circulating antibo titers.[2,3] High initial titers indicate more seve involvement. During therapy, as lesions resolve, t antibody titer will generally fall. A rising titer in spite treatment may indicate the need for more aggressi therapy. Circulating pemphigus-like antibodies ha been found in patients with extensive burns,[4] penicill drug eruptions[5] and dermatophyte infections,[6] but low titer only and without associated tissue fixe antibodies.

Bullous pemphigoid is an acute or chronic, relative benign bullous diease which affects mainly elder patients. The clinical features may be similar to tho

Figure 2 Indirect immunofluorescence testing of patient serum

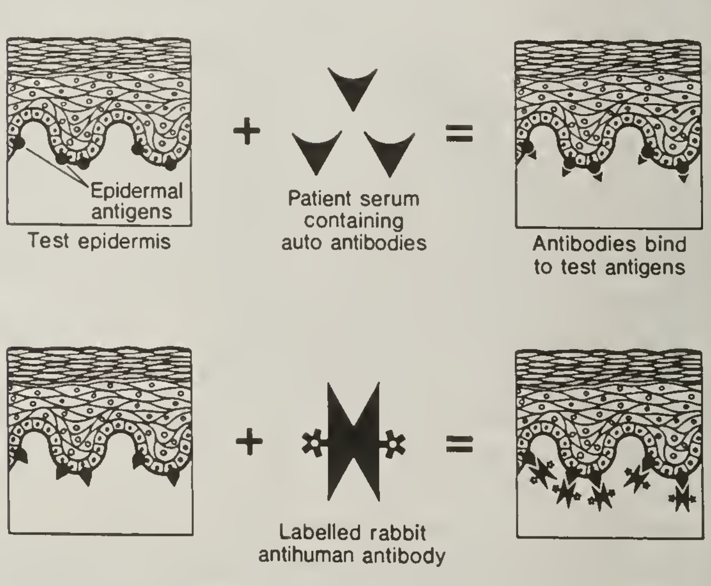
Epidermal antigens
Test epidermis
+
Patient serum containing auto antibodies
=
Antibodies bind to test antigens
+
Labelled rabbit antihuman antibody
=

Figure 2

From: Univ. of Arizona Health Sciences Center, Sect. of Dermatology (Dr. Levine), Dept. of Pathology (Dr. Nagle), Tucson, AZ 85724

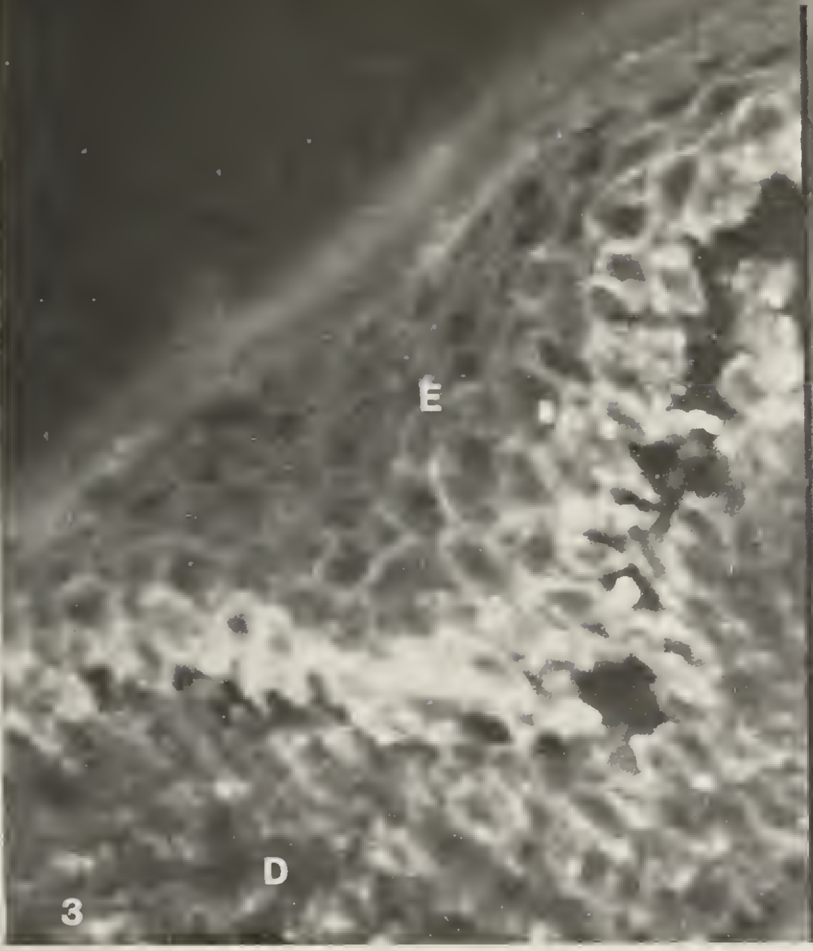

Figure 3
Cutaneous blister in pemphigus vulgaris demonstrating IgG antibody fixed to the surface of the epidermal cells (e) forming a fish-net like pattern

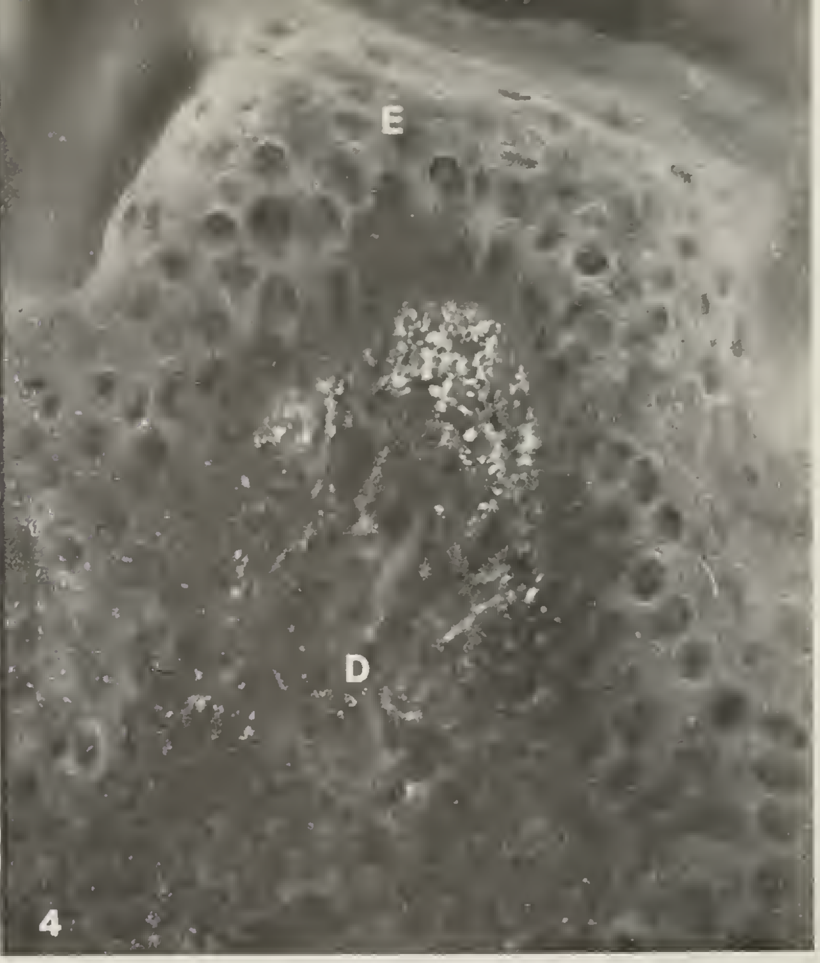

Figure 4
Cutaneous bulla in bullous pemphigoid demonstrating a linear band of IgG along the basement membrane zone between the epidermis (e) and dermis (d). Note fluorescence in both the roof and floor of the bulla.

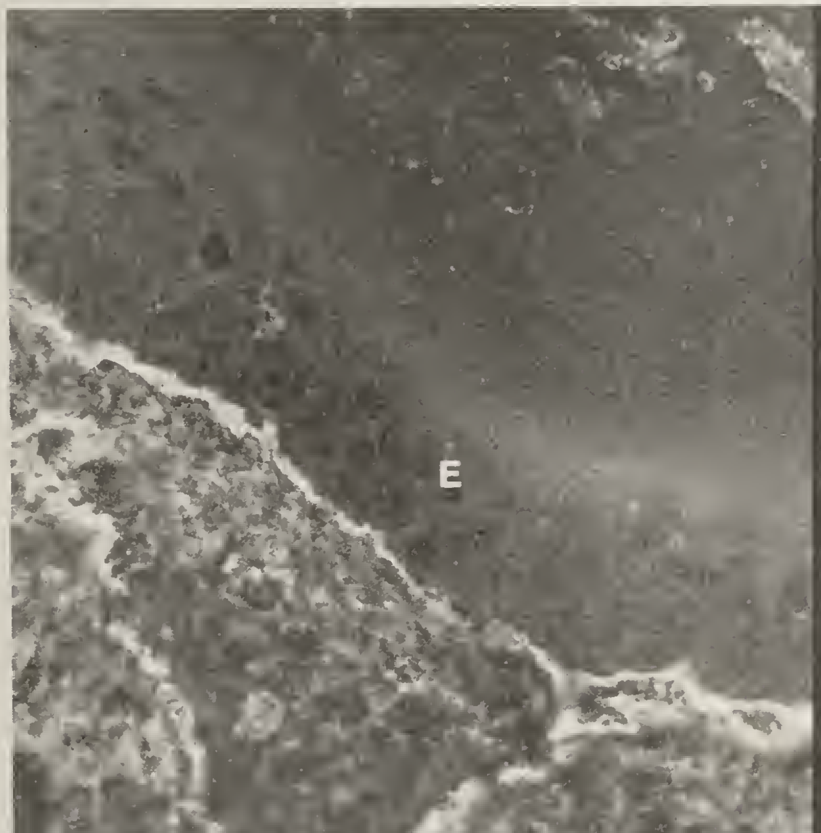

Figure 5
Perilesional skin in dermatitis herpetiformis with deposition of granular IgA in the dermal papillae (d) just beneath the epidermis (e).

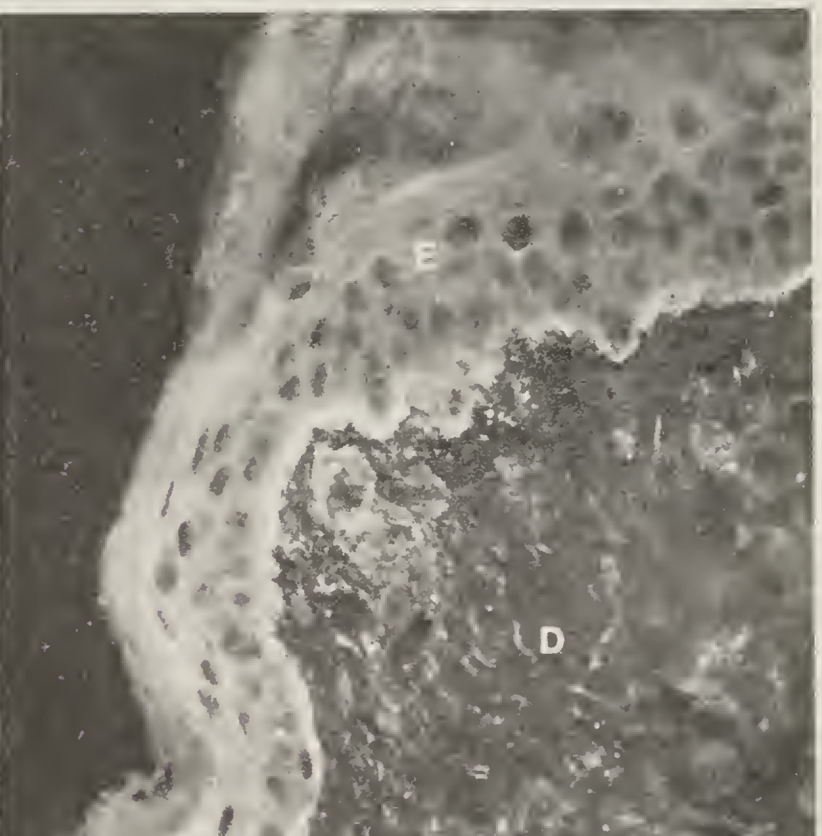

Figure 6
Lesional skin in lupus erythematosus demonstrating a granular band of IgG along the basement membrane zone between the epidermis (e) and dermis (d).

found in pemphigus vulgaris so immunofluorescence is helpful in differentiating the two diseases. In pemphigoid, direct immunofluorescence shows a linear pattern of complement and IgG along the basement membrane zone (Fig. 4) in skin adjacent to the bullae. Approximately 50% of patients also have a circulating anti-basement membrane zone antibody. The titers, however, do not correlate well with disease activity and so are not helpful in assessing therapy.[7]

Dermatitis herpetiformis is an intensely pruritic papulovesicular process which usually occurs symmetrically over extensor surfaces. It is difficult to distinguish this disease from other pruritic diseases on clinical grounds alone. A definitive diagnosis can be made with direct immunofluorescence examination of perilesional skin which shows granular dermal papillary IgA deposits (Fig. 5). No other disease has IgA deposits in this location. A linear IgA basement membrane zone pattern has also been described.[8] In dermatitis herpetiformis circulating anti-epithelial antibodies are not detectable.

The diagnosis of lupus erythematosus is often very difficult because there is no single criterion which is pathognomonic. Frequently, the patients will manifest several suggestive signs but not fulfill the American Rheumatism Asssociation criteria for the diagnosis of SLE. Immunofluorescent tests provide useful information in diagnosing this disease. The anti-nuclear antibody test (ANA) is an indirect immunofluorescent assay which detects serum antibodies to nuclear antigens. It is not specific for SLE but a titer of 1:160 or greater is suggestive of the diagnosis.[9] Lupus confined to the skin (discoid LE) may also have a positive ANA but the titer generally is lower.[9] The pattern of antibody deposition on the test nuclei may also aide in diagnosis. A peripheral nuclear pattern of staining suggests SLE, a speckled nuclear pattern occurs in the mixed connective tissue variant of SLE while a nucleolar pattern is characteristic of scleroderma. The homogenous pattern which is the most common one is not specific for any diagnosis.

The lupus band test (LBT) is a direct immunofluorescent technique used for detecting linear immunoglobulin deposition at the dermoepidermal junction in the skin of patients with lupus. The pattern may be either homogenous as in pemphigoid or finely granular (Fig. 6). In lesional skin, this is not pecific for LE, but in uninvolved, sun-protected skin, a positive LBT is very suggestive of SLE. A positive LBT has also been described in patients with a positive ANA and nephritis as the only manifestation of their disease.[10] Presumably, these patients have LE confined to a single organ, the kidney.[10] Some studies suggest that a positive LBT in uninvolved skin with IgG alone or IgG and other immunoglobulin classes is correlated with the presence of renal disease[11] while others dispute this claim.[12]

The diagnosis of certain cutaneous infectious diseases may be greatly aided by immunofluorescence studies. This is certainly true in syphilis where the Fluorescent Treponemal antibody (FTA-Abs) test has become th standard confirmatory test for present or past lueti infection. The test is performed by absorbing out of th patient's serum antibodies against non-pathogeni strains of treponemes and then performing indirec immunofluorescence with T. pallidum as the tissu substrate. The test is positive in 90% of patients wit positive darkfield examinations[13] and frequentl antedates a reactive VDRL. It's chief value is i confirming the diagnosis of syphilis in patients with reactive screening serologic test. The two mai problems with the FTA-Abs test are that it may remai positive for years after therapy, so cannot be used i patients with recurrent syphilis and rare biologic fals positive reactions may occur in lupus erythematosus,[14] pregnancy and protein abnormalities.[15]

In a few reference laboratories, immunofluorescenc is widely used to diagnose a number of other cutaneous infectious diseases. These tests all rely on the detectior of serum antibodies to the organisms using dried organisms as the tissue substrate. Current research suggests that soon a widely available gonorrhea test antigen may be available which would greatly improve the diagnostic accuracy in this disease since it has been demonstrated that a large percentage of patients with gonorrhea do develop serum antibodies against the organism.

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Range-gated Doppler Ultrasound:
A Review of its Utility in Clinical Cardiology

Zoe D. Kececioglu
Stanley J. Goldberg, M.D.
Hugh D. Allen, M.D.
David J. Sahn, M.D.

Introduction

The use of diagnostic ultrasound in medicine has grown rapidly in recent years because of its effectiveness as a noninvasive method of obtaining organ images. Ultrasonic imaging has been used to determine the size and nature of soft tissue organs such as the eye, abdominal viscera, and heart. However, this paper will focus on a new ultrasound technique for cardiac examinations, the combination of standard M-mode echocardiography and Doppler blood flow velocimetry.

This combination of techniques provides localized blood flow information from any desired area of the heart. The output can then be interpreted to detect cardiac abnormalities which cause disturbances in flow patterns.

In order to explain Doppler ultrasound as it applies to cardiology, we will review the basic physics of ultrasound and utilize two case studies to illustrate the diagnostic value of Doppler ultrasound. Finally, the major diagnostic limitations of Doppler ultrasound will be discussed. The intent is to indicate the present status of Doppler ultrasound in diagnostic cardiology.

The Physics of Doppler Utlrasound

Ultrasound is a term applied to high frequency sound. Sound energy exists in the form of waves analogous to those produced when a pebble is dropped into a pool of water. These concentric waves move outward from the disturbance created by the pebble where the peak of the wave corresponds to an area of molecular concentration. Molecules vibrate parallel to the direction of wave passage, thus alternating low and high pressure areas are formed. Piezoelectric crystals, which are ceramic disks, are able to sense these pressure waves and convert the mechanical pressure energy contained in them to electrical energy. Additionally, piezoelectric crystals have the ability to transform electrical energy into mechanical pressure energy.[1] These processes are similar to those demonstrated by a microphone which converts sound to electrical energy and a speaker which does the reverse. This energy conversion is frequently called transduction and is accomplished by a transducer which contains the piezoelectric crystal as its active element.

Figure 1 illustrates how an ultrasound transducer detects a boundary between two different materials, medium one and medium two. Since the materials are different, the probability is high that certain characteristics such as density and the velocity at which sound will pass through the medium will be different. These two quantities define acoustic impedance:

$$\begin{array}{c}\text{acoustic}\\\text{impedance}\end{array} = \begin{array}{c}\text{velocity of ultrasound}\\\text{in the medium}\end{array} \times \begin{array}{c}\text{medium}\\\text{density}\end{array}$$

If the acoustic impedance of medium one is the same as medium two, none of the ultrasound energy will reflect from the interface. However, if the acoustic impedance of medium one is different than that of medium two, some of the energy will be reflected at the interface and some will penetrate the interface.

Also in Figure 1, the wave pressure energy has been schematically depicted by arcs which represent maximal pressure concentration areas. The distance between any two consecutive areas is defined as one wavelength (λ), and the number of areas per second is frequency. Wavelength is an important consideration in ultrasonic work since it determines the degree of depth penetration. The reason for this occurrence is that

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From: University of Arizona Health Sciences Center, Department of Pediatrics, Tucson, AZ 85724. Reprint requests to Dr. Goldberg.

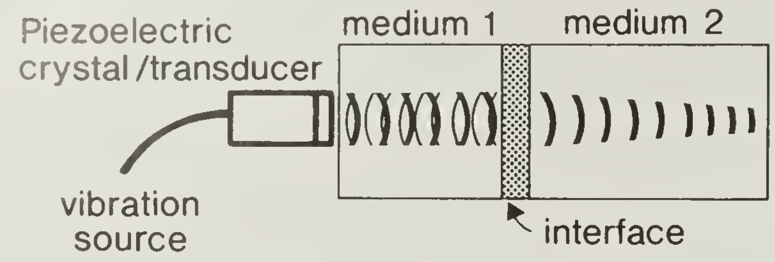


Figure 1
Ultrasound Structure Detection
An illustration of ultrasound structure detection. See text.

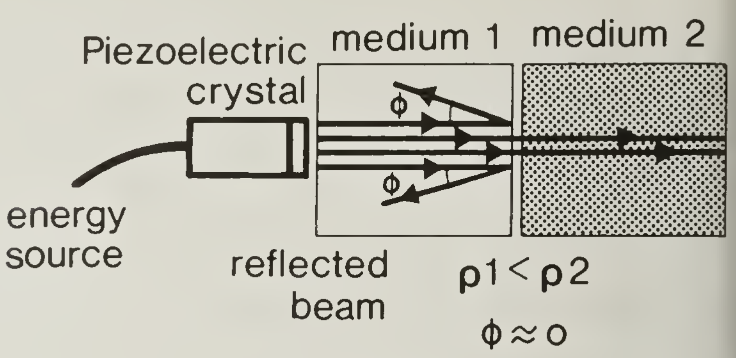


Figure 2
Ultrasound Beam Reflection
An illustration of ultrasound beam reflection. See text.

shorter wavelengths contain more energy than longer wavelengths. However, even though their energy content is greater, shorter wavelengths do not penetrate to as great a depth as longer wavelengths. Transmitted frequency determines the amount of structural detail that is obtainable by ultrasonic study. Therefore, an increased frequency which provides shorter wavelength and greater resolution results in reduced penetration. Thus higher frequencies are used to examine the hearts of smaller individuals where the need for detail is great but penetration requirements are minimal. Larger patients usually require use of lower frequencies, and thus some detail may be sacrificed for the necessary depth penetration.

Ultrasonic structure detection is possible only at the junction of two different tissues (i.e., muscle and blood interface) and only then if the acoustical impedance of the two structures is different. When tissue interfaces have impedances that markedly differ, a great deal of reflection occurs; but once an ultrasound wave has been reflected, it can no longer penetrate deeper body tissues. Figure 2 shows ultrasound beams entering a structure composed of two media with different acoustical impedances. At the interface, some of the energy is reflected by the interface at a small angle to return to the transducer. Once reflected, the beam cannot penetrate further. For example, 99.9% of the emitted energy is reflected when a soft-tissue/air interface is encountered. This means that structures located behind or within the lungs cannot be imaged ultrasonically. However, at a soft-tissue/soft-tissue interface (composed of tissues with different acoustical impedances) approximately 50% of the ultrasound beam is reflected thus leaving the remaining 50% for further penetration. Maximal ultrasound imaging occurs when the transducer is perpendicular to the cardiac structure as is the case in Figure 2. This is important since only the reflected energy which strikes the transducer will be sensed. Energy reflected so as to miss the transducer as the result of surface irregularities does not contribute to the ultrasound image. This is a problem since cardiac structures lie in many different planes, do not remain stationary, and assume irregular shapes. Accordingly, most reflected ultrasound does not return to th transducer, but some reflections do return and thes permit imaging of structures. Imaging can b accomplished either as one dimensional (M-mode) c two dimensional (cross-sectional) pictures both of whic accurately portray real time cardiac anatomy. Wall chambers, valves, and great vessels can be identifie measured, and observed. It is possible to obtain cardia images because of the varying distances that th structures lie from the transducer. The farther away th structure lies from the transducer, the longer it takes fo emitted ultrasound waves to be reflected and returne Reflections from cardiac structures which are close t the chest wall require a lesser amount of time to reac the transducer. This concept is the basis for th production of the various cardiac structure images.

Doppler Ultrasound Concepts

Doppler ultrasound has the advantage that bot cardiac structures and blood flow profiles can be studie The basis of this analysis method is the Doppler effec The Doppler effect is a change in the observed frequenc of a wave due to the motion of the source or target.[2] Fo example, consider a person (stationary target) standin by the railroad tracks of an approaching whistling moving train (source); the pitch of the whistle woul increase as the train moved closer and would decrease a the train passed the person and moved in the opposit direction. For ultrasound purposes, the stationar source is the piezoelectric crystal transducer and th moving target is a red blood cell in the heart or grea vessels. Figure 3 illustrates the Doppler effect for thi ultrasonic situation. Panel 3a shows the red blood cel moving toward the transducer source and encounterin ultrasound waves more quickly than if it were at rest This causes an apparent increase in source frequenc which is analogous to the higher pitch of the trai whistle upon approach. The increasing frequency i defined as a positive Doppler shift. Panel 3b depicts a re blood cell moving away from the transducer source thu encountering fewer ultrasound waves. This situatio parallels the lower apparent pitch of the train whistle a the train moves away from the person. A decreasing frequency is defined as a negative Doppler shift.

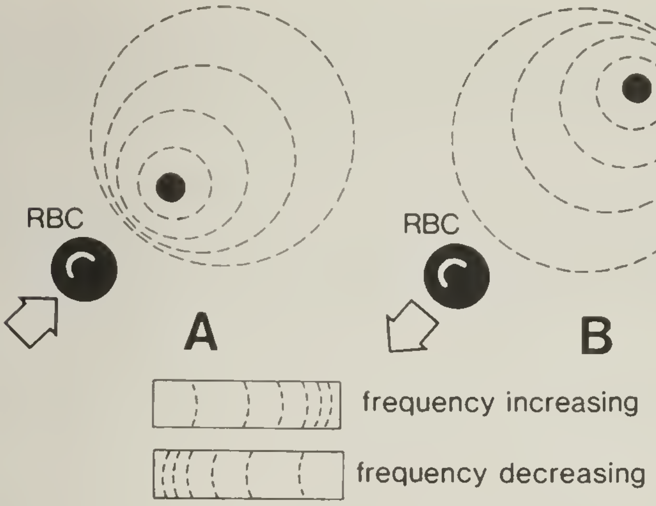


Figure3
Doppler Effect
An illustration of the Doppler effect. See text.

Doppler ultrasound equipment detects frequency shifts and thus determines the direction of red blood cell flow with respect to the ultrasound beam.

An important feature of Doppler ultrasound equipment is that it can localize red blood cell Doppler shifts to specific areas of the heart. The operator can select the observation area through the use of a movable range-gate. The ultrasound beam images structures to define location and the range-gate permits selection of a specific area of interest for velocity analysis. The positioned range-gate then allows study of flow of a volume of blood (called a sample volume) which is approximately 2 by 4 mm and teardrop shaped.

Once the cardiac structure and blood flow information has been received by the transducer, it is electronically processed into three forms: electrocardiogram (ECG), cardiac structure, and Doppler flow velocity. Figure 4 is an example of the output obtained from a Doppler ultrasound examination. The electrocardiogram is used for timing cardiac events. The cardiac structure information is obtained from the ultrasound waves which are reflected from the cardiac structures as previously explained. Doppler flow velocity information is processed to be evaluated in two forms: audible frequencies corresponding to the magnitude of Doppler shifts produced by red blood cells, and a graphical display of Doppler frequencies known as a frequency analysis (FA). The vertical axis of the frequency analysis represents Doppler shift frequency while the horizontal axis represents time. This frequency analysis measures blood flow velocity. Therefore, the frequency analysis and thus velocity measurement is done on a real time basis with the plotted points corresponding to flow characteristics in the heart at the time of observation. The distance the points are plotted above or below the zero frequency shift horizontal baseline indicates the magnitude of velocity and Doppler shifts. The points furthest from the baseline represent the larger Doppler shifts and thus the highest red cell velocities. All points located above the baseline indicate a positive Doppler shift meaning that the red blood cells are moving toward the transducer. Conversely, all points plotted below the baseline indicate a negative Doppler shift and this means that the red blood cells are moving away from the transducer. In Figure 4, the range-gate (rg) has been positioned to sample flow in the aorta (AO). The resulting frequency analysis is composed mainly of points plotted in the positive Doppler shift region as flow is toward the transducer.

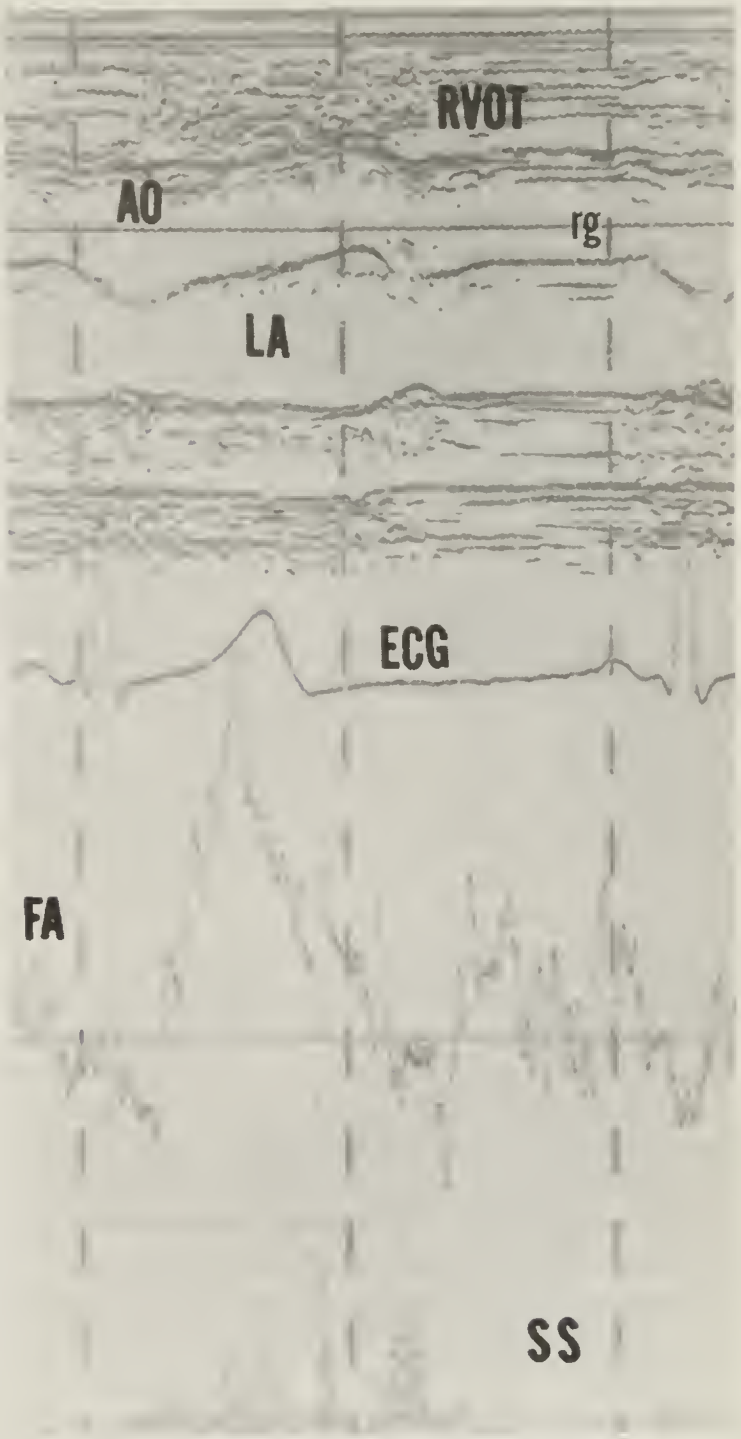


Figure 4
Doppler Tracing
This Doppler tracing was obtained from a normal patient and illustrates the M-mode (cardiac structure), ECG, and Doppler (flow profile) output information. The solid horizontal line represents the range-gate (rg); which indicates that aortic flow is being sampled. The frequency analysis (FA) is composed primarily of positive Doppler shifts indicating flow toward the transducer. The signal strength (SS) is properly adjusted as indicated by the presence of peaks and valleys in the profile.

One last piece of information which appears at the bottom of Figure 4 is the Doppler ultrasound output signal strength (SS). The signal strength relates how much raw Doppler signal is being processed. The signal strength is operator adjusted so that a profile of peaks and valleys is present as demonstrated in Figure 4. The peaks represent actual Doppler signals and the valleys indicate that noise is not a significant factor.

Diagnostic Doppler Technique

Transducer placement is a most important consideration in the performance of a Doppler ultrasound examination. When the transducer is positioned on the chest (precordial placement), most cardiac structures are accessible by transducer angling. The transducer may also be placed in the suprasternal notch (suprasternal placement) to image the transverse aortic arch, right pulmonary artery, and left atrium. However, it should be realized that the ultrasound beam must be directed in one manner for optimal cardiac structure imaging and another for Doppler flow information. As mentioned earlier, the best cardiac structure images are obtained by directing the transducer perpendicular to the structure. This is advantageous because the majority of the reflected, returning ultrasound waves will strike the transducer instead of being angled off in another direction. The best Doppler velocity information is obtained by achieving an angle of 180 degrees between the ultrasound beam and blood flow. Placing the transducer at this angle insures that the red blood cells transmit a maximal Doppler shift to the transducer rather than a suboptimal Doppler shift as would be obtained if the ultrasound beam intersected blood flow at a lesser angle. In most instances, an angle of 180 degrees is impractical thus a lesser angle must be accomplished. If an angle of 180 degrees between the Doppler transducer and the blood vessel were possible, volume blood flow measurements could be obtained since the angle would be known. The preceeding discussion then leads to the conclusion that a compromise must be made between the optimal transducer angles for recognizable cardiac structure and Doppler flow information outputs. However, some cardiac areas can never by analyzed from prime transducer angles due to their position within the body.

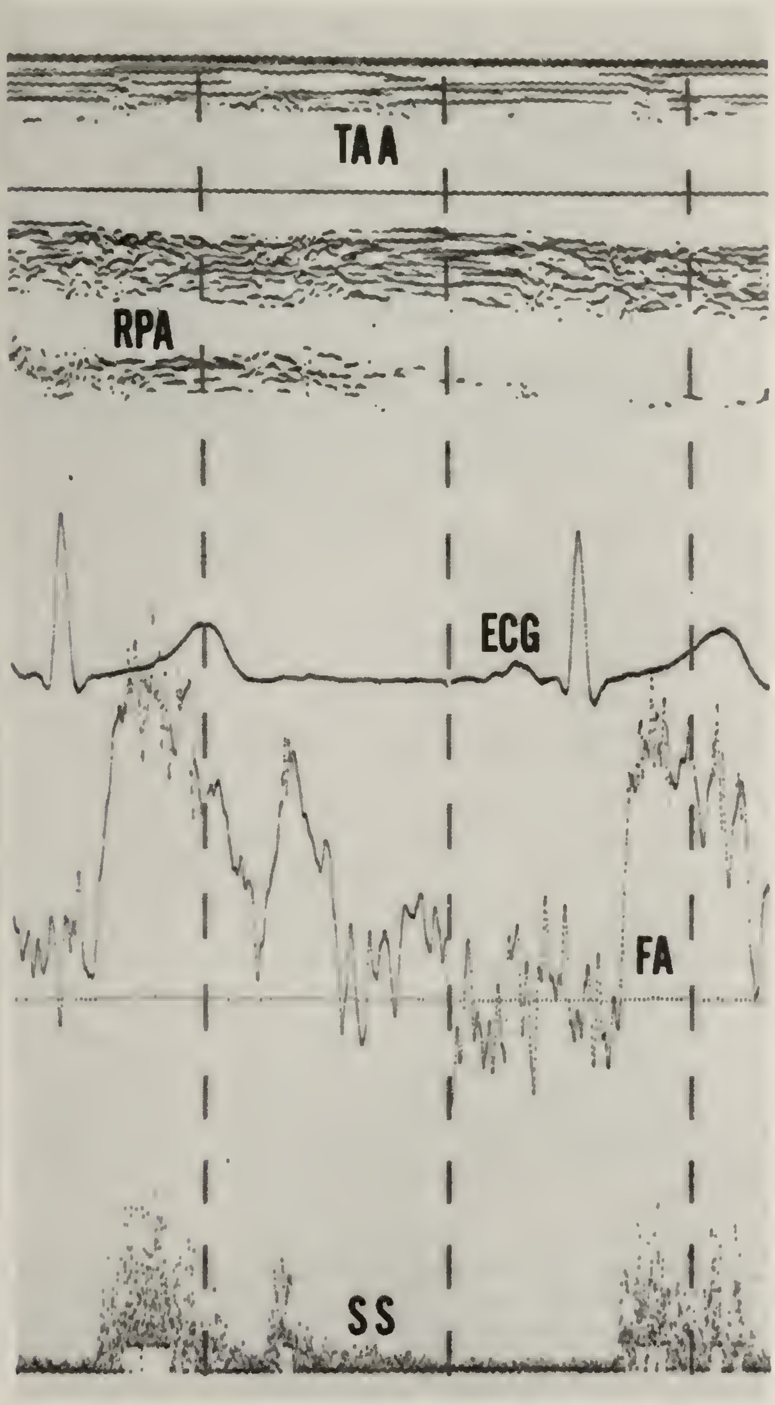
Doppler ultrasound can be used diagnostically if the cardiac lesion present produces a change in flow characteristics. This change may appear as an abnormal flow direction or, more commonly, by producing a flow disturbance. In normal patients, smooth or laminar flow is present in cardiac chambers and great vessels. Laminar flow means that at any point in time and in a given location, the red blood cells are moving in the same direction at a generally similar velocity. The Doppler frequency analysis for this case will show velocity curves which are generally smooth and formed by closely spaced points. Figure 4 demonstrates the frequency analysis profile obtained when the red blood cells exhibit similar magnitude Doppler shifts due to laminar flow. However, non-laminar or disturbed flow results when red blood cells move in random directions due to eddies caused by a circulatory obstruction. When the ultrasound beam is reflected from chaotically moving blood cells, the result is a scattering of points on the Doppler frequency analysis. This occurs with disturbed flow since the blood cells move simultaneously toward and away from the transducer at various velocities. Figure 5b is a Doppler output obtained from a child with a cardiac lesion showing the random Doppler shifts caused by chaotic motion of the red blood cells.

When interpreting Doppler information, a four step thought sequence is followed in order to completely analyze the received data:

1. M-mode cardiac structure orientation
2. Doppler range-gate position
3. Doppler frequency analysis interpretation
4. Electrocardiographic timing.

Two case studies will be utilized in order to demonstrate applications of this analytical method.

Figure 5a is the transverse aortic arch Doppler study of a normal and 5b is a Doppler tracing obtained from an 8-year old child who has aortic stenosis. Using the four step analysis method, the thought process followed to arrive at this diagnosis will be demonstrated. Examination of the cardiac structure output indicates that the tracing resulted from suprasternal placement of the transducer and first imaged the transverse aortic arch (TAA), the right pulmonary artery (RPA) deep to the TAA, and the left atrium (LA) deep to the RPA.[3] The range-gate (rg) is depicted as a straight horizontal line on the M-mode portion of the tracing. In this instance, the range-gate has been positioned in the transverse aortic arch. The Doppler frequency analysis (FA) indicated a wide dispersion of vertical points which indicates flow disturbances caused by a left ventricular obstruction. The electrocardiogram shows that the point dispersions occur during systole. All forms of aortic stenosis result in transverse aortic arch systolic turbulence. In patients with aortic valvular stenosis, disturbed systolic flow should also be detected above the aortic valve orifice. Detection of flow disturbances just above the aortic leaflets or in the transverse aortic arch is consistent with aortic stenosis, but the obstruction could also be below the aortic valve. To prove that the obstruction was valvular, the operator should show laminar flow below the aortic valve. This localizes the problems to the aortic valve. An important point is that once a smooth flow has been transformed into disturbed flow by an obstruction, the flow remains disturbed until the blood is no longer moving. This means that dispersions must be traced to their origins to reach a valid conclusion. In Figure 5b, the disturbed flow in the transverse aortic arch originated at the aortic valve and continued into the aorta. The disturbed flow may not persist far beyond the transverse aortic arch due to frictional losses or flow cessations in diastole. For these



reasons, the disturbance does not appear in the femoral artery.

Figure 6a is the Doppler tracing of the right atrial outflow tract of a normal child and Figure 6b is the Doppler tracing which was obtained from a 6-year old child who had an atrial septal defect. The atrial septal defect may be suspected through careful study of the Doppler output.[4] Cardiac structural evaluation indicates that the area of study is the right atrial outflow tract indicated by tricuspid valve leaflet (tl) presence. The Doppler range-gate (D) is depicted as the horizontal line in the right atrial outflow tract. the Doppler frequency analysis reveals an obvious flow disturbance in the sampled area. Electrocardiogram assessment shows that the point dispersions occur during diastole. All of the preceeding observations point toward the presence of excessive flow through the right atrial outflow tract. However, detection of this flow disturbance in the right atrial outflow tract is a secondary diagnostic characteristic since little or no flow disturbance occurs at the site of the large atrial defect which allowed this low pressure shunt. The reason that a disturbance occurs in the right atrial outflow area is that all of the normal venous return plus all of the shunted blood must pass through the tricuspid valve. Accordingly, the volume is large and the flow velocity is high, so high that smooth flow is changed to disturbed flow.[5] Therefore, to suspect this condition, flow must be sampled in the right atrial outflow tract.

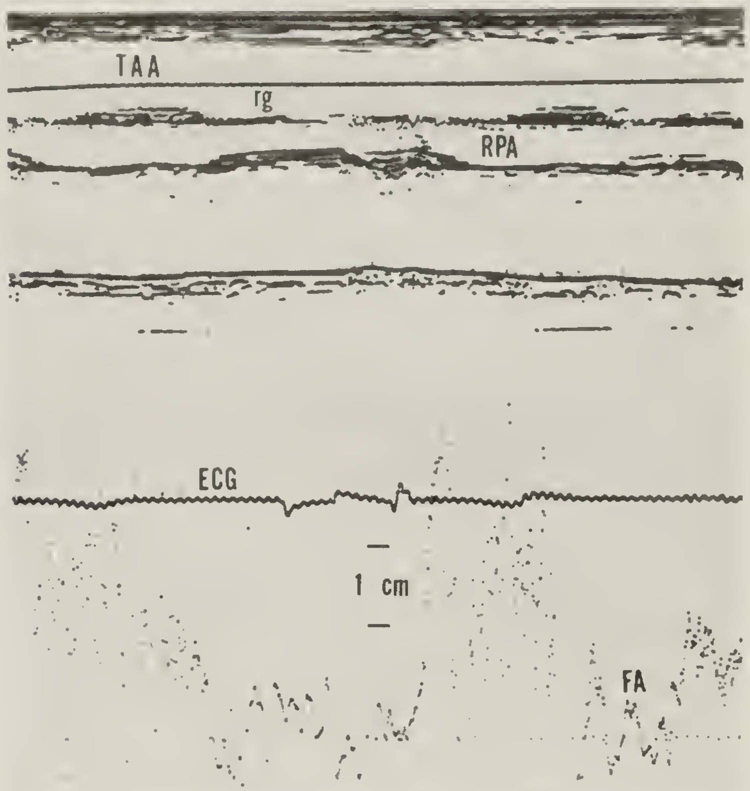


Figure5
Aortic Stenosis
Doppler tracing B illustrates flow disturbances present in the transverse aortic arch of an 8-year old child diagnosed with aortic stenosis. This disturbed flow profile can be compared with Doppler tracing A which shows normal flow in the transverse aortic arch.

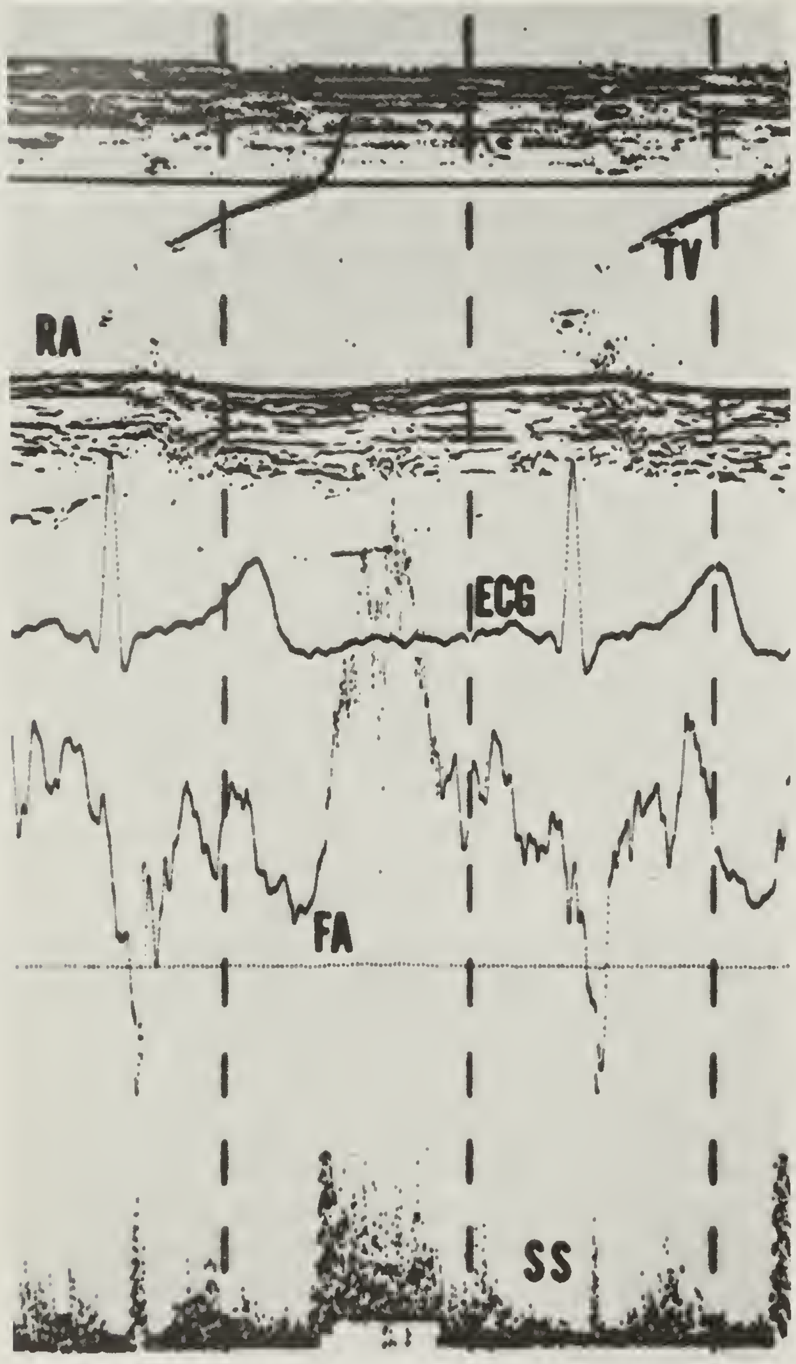
The preceeding cases demonstrate examples of the manner in which Doppler ultrasound is diagnostically utilized. The same analytical method can also be employed to diagnose the presence of other cardiac abnormalities that produce flow disturbances.

Doppler Ultrasound Limitations

While Doppler ultrasound is a promising method used to aid in the detection of cardiac abnormalities, the technique does have limitations. These limitations fall into four categories:

1. Doppler range-gate locator limitations
2. Doppler flow and cardiac structure output interpretation limitations.
3. Doppler ultrasound equipment limitations
4. Doppler ultrasound operator limitations.

The Doppler range-gate locator limitations arise because at times it is difficult to determine exactly where the range-gate is sampling blood flow. Similar problems arise when it cannot be determined exactly which cardiac structure has been imaged. These problems can be overcome with experience. The last two limitation categories deal with the inability of the Doppler



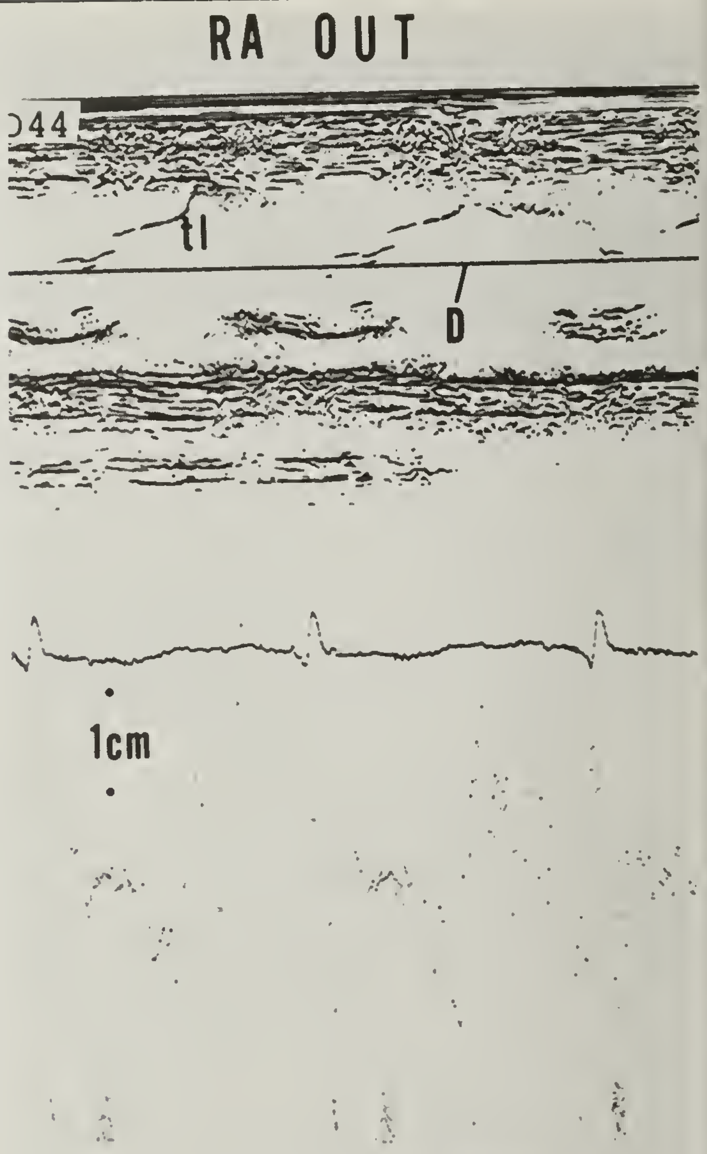


Figure 6
Atrial Septal Defect
Doppler tracing B illustrates the flow disturbances present in th right atrial outflow tract of a 6-year old child with an atrial septa defect. This disturbed flow profile can be comapred with Dopple tracing A showing normal flow in the right atrial outflow tract.

ultrasound equipment or operator to produce accurate, quality output. As Doppler ultrasound is in its infancy, new equipment is rapidly entering the market making the production of quality recording a reality. However, the usefulness of a Doppler ultrasound examination still depends upon the skill of the operator.

Conclusions

Aside from the limitations inherent in range-gated Doppler use, there are several advantages to this method of obtaining cardiac information. The major advantage is that Doppler equipment provides noninvasive flow velocity information for a specific area of the heart. Although a stethoscope may be used to detect flow disturbances, it must be appreciated that a stethoscope detects flow disturbances that are heard in varying intensities from all regions of the chest, the intensity change being principally a function of distance from the source. Therefore, more localized cardiac structure information and blood flow information are obtainable only with range-gated Doppler. Additionally, a Doppler ultrasound examination may be conducted practically in any area of the hospital and as often as desired on the same patient with no detrimental effects Although the technique is still relatively new, its clinica qualitative utility is considerable and many ne quantitative advancements lie in the near future a Doppler is presently being interfaced to cross-sectiona imaging equipment. The combination.of these device will allow precise knowledge of the angular relationshi of the Doppler beam to flow. Knowledge of that angl and the velocity measured by Doppler should permit accurate noninvasive measurement of volume blood flow within the cardiac chambers and great vessels.

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Aids in the Diagnosis of Multiple Sclerosis

Colin R. Bamford, M.D.
William A. Sibley, M.D.
Jose F. Laguna, M.D.
James P. Ganley, M.D.

Abstract

In spite of an awareness of the incidence and manifestations of multiple sclerosis, the physician is often frustrated by the elusiveness of proof that the disease exists in some cases. This article describes newer techniques currently used to confirm or support the diagnosis, and provides several case reports in which the techniques were used for this purpose at the Health Sciences Center. The four methods described include the Visual Evoked Response, the Somatosensory Evoked Response, Computerized Axial tomography and a modified Ophthalmological examination consisting of fluorescein angiography, and indirect ophthalmoscopy with scleral identation.

In this article we shall describe the newer methods of establishing the diagnosis of multiple sclerosis and comment upon their practical use by the clinican. These methods, however, are not a substitute for the conventional clinical criteria used to make the diagnosis, but should be considered complementary and can be of great value in some instances.

Classically, we think of multiple sclerosis as a disease which develops in young adults and manifests itself as episodes of deterioration followed by partial or complete improvement, culminating after many years in the development of significant disability. It is a sobering thought that only 26% of the patients being followed at the Health Sciences Center MS clinic are currently following this course. A further twenty-six percent of our patients have an insidiously progressive deterioration of neurologic function such that they remark only on their inability to do things as easily as they had been able to the previous year. These complaints may be referrable to walking, eating and other activities of daily life. The remainder of the patients at present have an inactive disease with no apparent change being observed on repeated examinations over a period of several years.

An analysis of the patient's course may allow us to determine that the patient has a disease "disseminated in time."

The neurologic examination should be used to demonstrate that more than one tract within the central nervous system is affected ("disseminated in space"), and if multiple tracts are involved they are not tracts which are adjacent to each other. Thus, if a spinal cord and optic nerve lesion can be demonstrated, the criterion has been adqequately met.

If these critera are rigidly required for the clinical diagnosis of MS, then a percentage of patients with the disease of MS will be undiagnosable clinically. To underscore this point the diagnosis has been subclassified[1] to include 1) clinically definite multiple sclerosis, 2) probable multiple sclerosis, 3) possible multiple sclerosis and even 4) subclinical multiple sclerosis.

Major difficulty in establishing the diagnosis of MS is found in the patient with 1) very early disease, i.e., when only one attack has occurred, 2) in mild disease, when the disability and signs of the disease have resolved, 3) in patients with subjective symptoms similar to those complained of by hysterical patients, and which are unaccompanied by objective neurologic signs, 4) in patients who have disease courses atypical for MS and appearing to mimic other neurologic diseases, and 5) in patients who due to dementia are unable to provide an adequate past history or an accurate description of present symptoms. It is in these 5 categories of patients that the new techniques have the greatest value.

The Visual Evoked Response (VER)

As early as 1934, Adrian and Matthews[2] demonstrated that a flashing light placed in front of a patient's eyes, could trigger occipital rhythms at the same frequency.

In 1970 Halliday and Michael,[3] showed that a reversing checkerboard pattern could be used to stimulate the retina instead of a flashing light, and the induced occipital waveform became more reproduceable. The time that it took for the stimulus to induce the waveform could be measured, and this too was found to be reproduceable in the same patient.

The basic concept is that light enters the eye, is transduced into electrical energy by the retinal cells, and these electrical impulses are transmitted via the optic nerves, chiasm, tracts and radiations to the occipital lobes, where a proportinate number of neurons discharge, producing an electrical field detectable at the scalp using EEG electrodes. This electrical wave is called a visual evoked response.

If the light is directed into one eye, the impulse passes through the ipsilateral optic nerve, however once it reaches the optic chiasm the impulse splits and follows both pathways to the occipital lobes. Once the impulse has diverged, the existence of an alternate route results in some technical difficulty in detecting uilateral (post-chiasmatic) lesions. For this reason the visual evoked response can be used easily and reliably to measure

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From: Univ. of Arizona Health Sciences Center, Dept. of Neurology, Tucson, AZ 85724. Reprint request to Dr. Bamford.

function in the optic nerve. It can also be used to determine the function of the better of the two post-chiasmatic visual pathways.[4]

How does multiple sclerosis interfere with the V.E.R.? Multiple Sclerosis causes demyelination, and this interferes with nerve conduction in two ways, the milder being slowing of transmission of the nerve impulse, the severer being a complete blocking of the nerve impulse. Slow transmission through the optic nerve results in a prolonged latency from the time of stimulation to the time that the wave is recorded from the scalp. Blocking results in the absence or severe attenuation of the amplitude of a visual evoked response.

A delayed V.E.R. is not specific for MS, it implies a lesion of the optic nerve. It's use in the diagnosis of MS is particularly valuable when the patient has a dubious or no hisotry of optic neuritis, normal visual fields, normal visual acuity, or an impaired visual acuity attributable to other ocular problems (problems not affecting the optic nerve viz. refractive, cataracts, etc.).

Over 95% of patients with clinically definite multiple sclerosis have been shown to have a delayed V.E.R., even though only 50% of these patients had a prior history of optic neuritis.[4]

Case 1: A 26 year old female, when she was 16, developed an attack of weakness and numbness of the legs following a bee sting. This lasted 3 days. When 18 she had a recurrence of leg numbness which lasted 3 months. At 19, she developed an electrical shock like sensation on flexing the head, (L'hermitte's sign) followed two months later by blurred vision on the right, a visual acuity of 20/50, and normal visual fields. At 22, she was admitted with complaints of numb legs, difficulty breathing and swallowing. There were no objective neurologic signs. Emotional instability was considered to be either completely or partially responsible for the admission. When she was 23 she was readmitted with complaints of numbness of the hands and legs, a Babinski reflex was transiently obtained by one examiner, however, there was a disparity between many aspects of her neurologic examination e.g., her ability to walk without difficulty, accompanied by profound weakness of the knees and the absence of position sense in the legs. At the age of 26 she was admitted with a L'hermitte's phenomenon, headaches and numbness. Her cranial nerve examination was intact. Strength was normal, deep tendon reflexes were 2+ and equal, except for the knee jerks which were 4+ and equal bilaterally. Plantar responses were neutral. There was a decrease in sensation to pain and light touch, distributed in patchy bands around the trunk. Position sense was absent at both great toes, vibration sensation was intact over all 4 extremities. Coordination was intact. A L'hermitte's sign could be elicited. During the hospitalization the patient was observed to hyperventilate on one occasion, and on another to have hallucinations. Visual evoked responses were preformed and were abnormally prolonged bilaterally (OS 115 msec, OD 114.6 msec, Control <110 msec.). See Figure l.

Visual Evoked Response

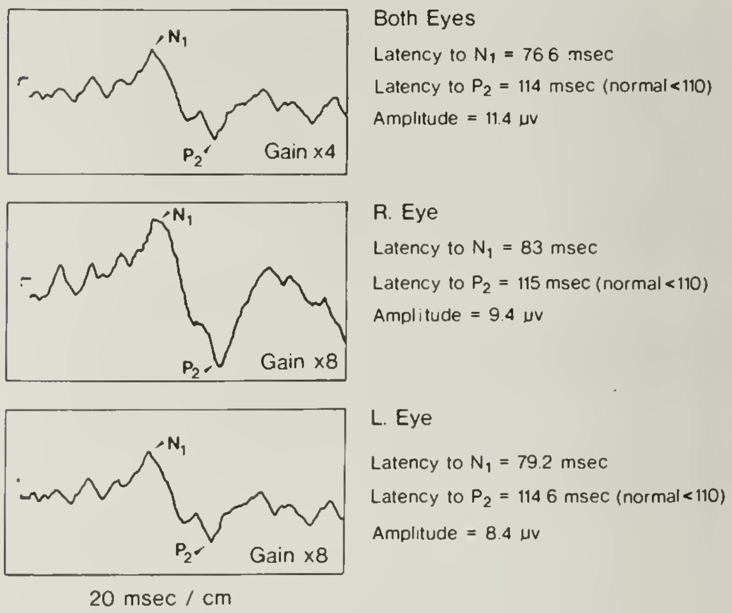


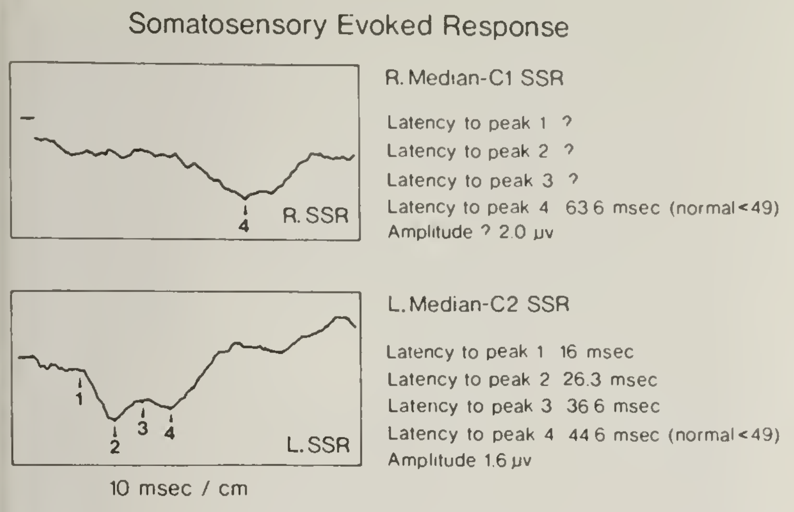
Figure 1

Comment: This patient has been followed conscientiously for many years, and in spite of numerous "exacerbations," failed to develop the typical objective neurologic signs which often accompany these symptoms. This accompanied by overt hysterical behavior, was unsettling to the clinican who requested a V.E.R., a test which was independent of the motivations of the patient. The abnormal result provided objective support for the history suggestive of optic neuritis.

The Somatosensory Evoked Response (SSR)

The procedure has many aspects in parallel to those of the V.E.R. The median nerve is electrically stimulated, the electrical impulse is transmitted via the peripheral nerve, spinal cord and brainstem to the sensory area of the opposite cerebral hemisphere, where it induces a reproduceable waveform. The time that it takes for the impulse to pass from the median nerve to the cerebral cortex is constant in the same patient, and the normal range has been well documented.[5] A prolongation of this time (or latency) implies dysfunction along this pathway. Prior to requesting or performing this study, a reasonable effort should be made to clinically exclude significant median nerve disease. Having done that it is reasonable to presume that slowing is due to delayed transmission through CNS white matter tracts, and an absence of the SSR is probably due to complete block of nerve transmission. Again, we caution that the SSR is delayed in the presence of different types of lesions such as demyelination or degeneration of tracts, and is not specific for MS.

Ninety-five percent of MS patients who had impaired vibration and position tests had abnormally prolonged SSR's.[5] In another study[6] 94% of patients with clinically definite MS had abnormal SSR's, and 37% of patients with possible MS had abnormal results. Thus the



R. Median-C1 SSR

Latency to peak 1 ?
Latency to peak 2 ?
Latency to peak 3 ?
Latency to peak 4 63.6 msec (normal<49)
Amplitude ? 2.0 µv

L. Median-C2 SSR

Latency to peak 1 16 msec
Latency to peak 2 26.3 msec
Latency to peak 3 36.6 msec
Latency to peak 4 44.6 msec (normal<49)
Amplitude 1.6 µv

Figure 2

procedure can be used to identify the presence of a second subclinical lesion, so that the criterion of 'dissemination in space" can be met.

Case 2: A 31 year old female had the sudden onset of right eye blindness in March 1978, which was treated with oral steroids. By May 1978 the vision had returned to normal. In August 1978 the vision of the left eye began to slowly deteriorate until in October 1978 there was no light perception. The left eye began to improve. In mid-October 1978 there was a recurrence of right eye blindness, associated with ocular pain aggravated by eye movement. The patient recalled having a tendency to fall towards the right in September 1978. On neurologic examination the patient had evidence of an optic neuritis on the right and optic atrophy on the left. The cranial nerves were otherwise intact. Motor function testing revealed normal strength, mildly increased tone of the legs, normal deep tendon reflexes, and normal plantar responses. Sensation and coordination were intact. Somatosensory responses were performed. The left median - C2 SSR was normal. the right median - C1 SSR ws abnormally prolonged, See Figure 2.

Comment: Aside from the dramatic ocular manifestations, the patient's neurologic review of symptoms and neurologic examination was unimpressive.

The clinician should not use each optic nerve as a separate site of neurologic involvement, when attempting to fulfill the criterion "dissemination in space," as a single lesion within or adjacent to the optic chiasm can produce bilateral blindness, and secondly there are many other non-MS conditions, which may have an impact on both optic nerves either simultaneously or separated in time.

Somatosensory responses in case 2 revealed the subclinical second tract lesion, confirming the diagnosis of multiple sclerosis.

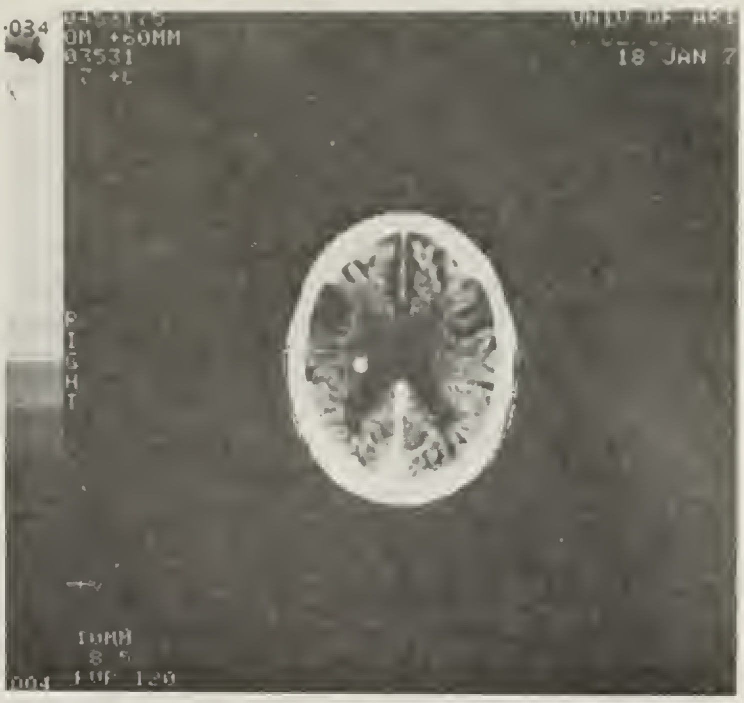


Figure 3

Case 3. Contrasted CT scan demonstrating a 1 cenimeter enhancing lesion in the periventricular area of the right frontal lobe.

The Computerized Axial Tomogram (CT)

CT scanning is a safe and painless method of obtaining a two dimensional view of the brain. Multiple views of the brain can be obtained in both the horizontal and coronal planes, so that the anatomy of the entire brain can be displayed in terms of coefficients of x-ray absorption. By intravenously injecting iodine containing compounds, the blood vessels may be visualized, and leakage of the agent through abnormally permeable vessels into the surrounding tissues may be seen. Patients who have recently presented with acute, severe exacerbations of multiple sclerosis often have a normal non-contrasted study, however, when contrasted, areas of enhancement may be seen to be located in the cerebral white matter.[7,8] With the passage of time these areas change to either normal or low density areas which do not enhance with contrast.[8]

In 33% of MS patients with disease of long duration low-density areas were noted in the periventricular areas, and these areas failed to enhance with the administration of a contrast agent. A large proportion (75%) of these patients were noted to have enlarged ventricles and cerebral atrophy. Less than 20% of these patients had normal CT scans.[9]

Case 3: A 52 year old female was referred from a nursing home for the purpose of excluding "a possible stroke," since the patient had been noted to develop a sudden ophthalmoplegia and facial weakness. The patient reportedly had developed numbness of her feet, shoulders and arms in 1959, which was attributed to multiple sclerosis. In 1960, she developed incontinence of urine, and by 1966 was wheelchair-bound. In 1976, she became bedridden and was constantly catheterized. She had been living in a nursing home for many years, and had become progressively demented during this time. On neurologic examination, the patient was moderately demented. She had a right gaze palsy and a left gaze internuclear ophthalmoplegia. A decreased left

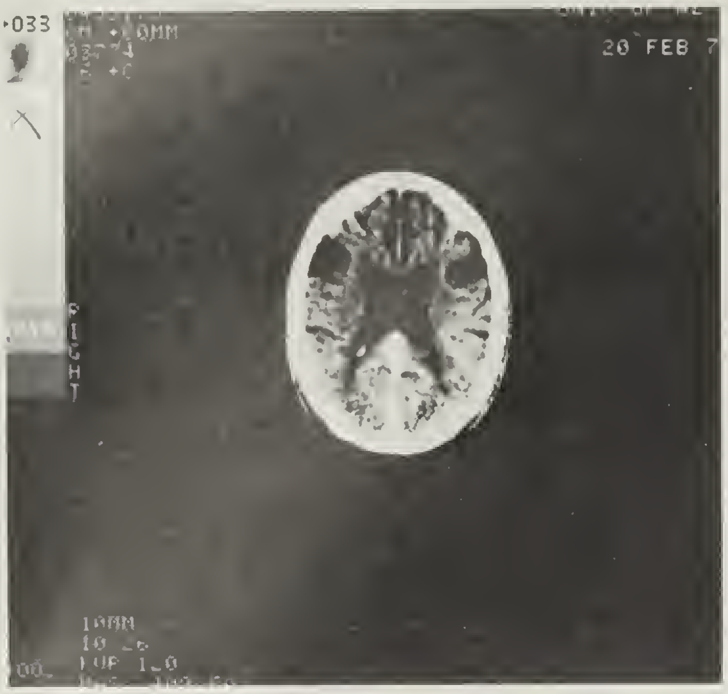


Figure 4
Case 3. Contrasted CT scan performed l month later than that shown in figure 3, the enhancement has disappeared, to be replaced by an area of low density.

corneal reflex was observed. The remaining cranial nerves were intact. Motor function testing revealed moderate weakness of the left arm and severe weakness of the left leg. Deep tendon reflexes were absent at the arms, the right knee jerk was 2+, the left 3+ , the ankle jerks were 2+ . Plantar responses were extensor. Sensory function testing was grossly intact except for an absence of position sense on the left and an absence of vibration at the ankles. Cooperation was limited. There was a mild intention tremor. The CSF was abnormal with 6 monocytes/cu. mm, a protein of 57 mg% and an IgG: total protein ratio of 43% (normal <15%). A contrasted CT scan performed shortly after admission revealed a 1 centimeter enhancing lesion within the deep right frontal lobe. This was surrounded by diminished density but there was no mass effect. See Figure 3. One month later, contrasted and non-contrasted CT scans were obtained. The previously enhancing lesion had disappereared and was replaced by an area of low density. See Figure 4. A similar lesion had in the interim developed deep within the left parietal lobe. See Figure 5.

Comment: Although the sudden onset of neurological deficit, and the distribtuion of neurological signs (right gaze palsy, left gaze internuclear ophthalmoplegia, and left heimparesis) was suggestive of a right paramedian pontine infarct, the CT scann demonstrated lesions elsewhere highly suggestive of active multiple sclerosis. It is highly probable that a plaque was present within the right pons, yet could not be seen because it was small and failed to enhance intensely.

Case 4: A 50 year old female had a history of having had a bout of left sided numbness at the age of 36, which lasted two weeks and then remitted. At 37 she developed tingling hands which also lasted two weeks. At 39 she noted difficulty with her legs, which tended to slowly deteriorate. At 47 she required canes, and at 50 a wheelchair. On physical examination her cranial nerve were found to be intact, her lower extremities wer mildly weak and moderately spastic; she had bilatera Babinkis and hyperreflexia; sensation was intact excep for inability to detect vibration at the ankles, an coordination was found to be moderately imparied. Th admission was prompted by depression, confusion incontinence, falling and intermittent low grade fevers The recognition and treatment of a urinary trac infection resulted in an improvement in the presentin symptoms, except for a persistent dementia. A computerized axial tomogram was performed to exclud a subdural hematoma, and as expected revealed th effects of longstanding MS viz. cerebral atrophy. See Figure 6.

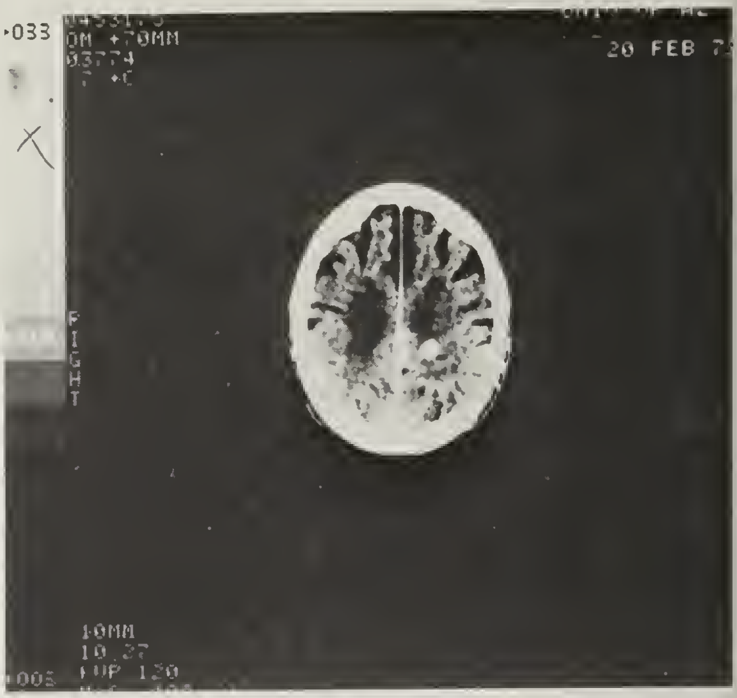


Figure5
Case 3. Contrasted CT Scan performed l month later than that show in Figure 3, a new area of enchancement 1.5 centimeters in diamete has now appeared in the left parietal periventricular area.

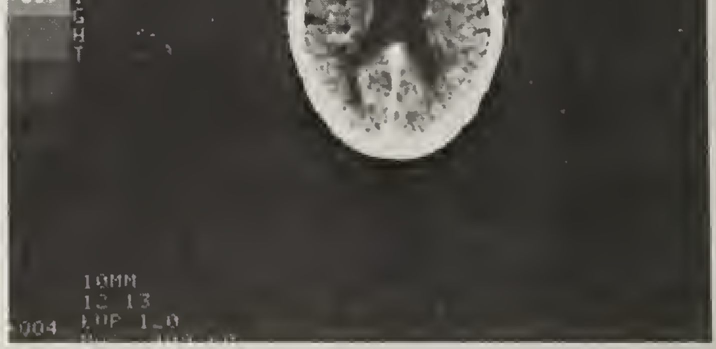


Figure 6
Case 4. Long-standing stable to slowly progressive MS case demonstrating ventricular enlargement and cerebral atrophy.

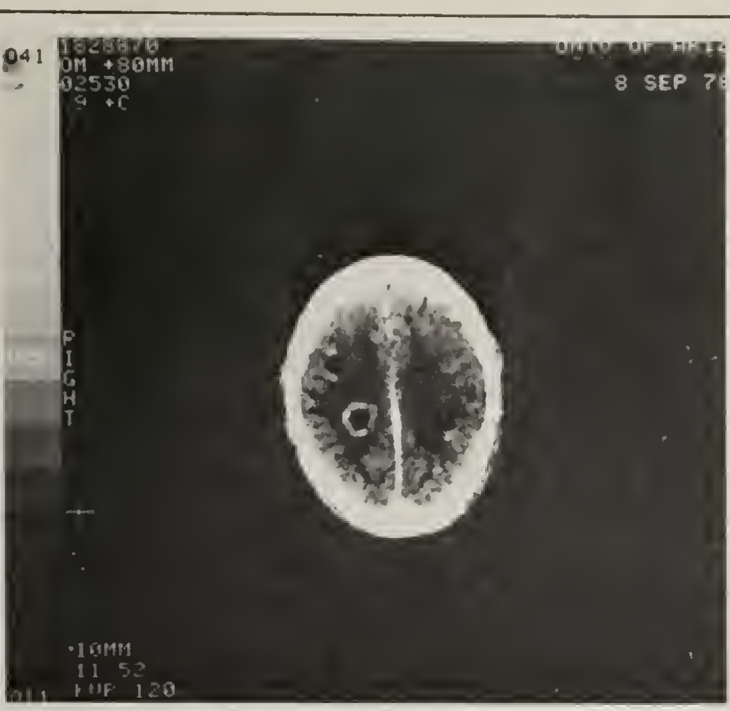


Figure 7
Case 5. Right frontal white matter ring-enhancing lesions.

Comment: The patient's course had varied from stability to very insidious progression. The recent deterioration of mental status and neurologic function was attributable to a urinary tract infection and in support of this the CT scan did not show any evidence of new MS activity.

The value of the CT scan in MS is greatest when one is faced with the problem of the patient with acute MS. These patients rapidly deteriorate and become severely disabled within weeks to months. Any improvement may be overshadowed by deterioration in other areas. The relentless progression may be frightening and frustrating. Although the signs may clearly imply white matter involvement, the differential diagnosis on admission often includes encephalitis, post-infectious encephalomyelitis, glioblastoma, etc. Correct interpretation of the CT scan will clarify the diagnosis and help exclude these other conditions. Although the following case report is not representative of acute MS, it does illustrate the dilemma that these patients present.

Case 5: A 31 year old white American female noted the onset of frontal headaches six months prior to admission. Two months prior to admission she began having vague complaints of dizziness. One week prior to admission she noted that she was unable to speak clearly, and in the next few days she complained of choking. On admission the patient was pleasant, cooperative and at ease. Vital signs and general physical examination were normal. Mental status was normal. Cranial nerve examination revealed nystagmus on lateral gaze bilaterally, weakness of the lower half of the face on the left, and dysarthria. Her strength was intact, but she had hyperreflexia on the left and bilateral Babinskis. Coordination and sensation were intact. A CT scan was performed which revealed multiple right frontal and parietal white matter ring enhancing lesions. See Figure 7. The CT was repeated at a later date and showed some improvement. An arteriogram revealed a few minor irregularities of unclear significance. The patient was discharged in an unchanged condition after a 4 day hospitalization, and two weeks later the patient felt that she was improving although she still complained of severe fatigue. Six months later the patient was asymptomatic, and a repeat CT scan showend non-enhancing lucencies in the (R) hemisphere, which had significantly improved since the initial study.

Comment: This history of headaches, followed by dizziness, dysarthria and choking resulted in the admitting diagnosis of a brain tumor. The CT scan showed multiple ring shaped lesions which enhanced with contrast, and were localized in the cerebral white matter. The lack of mass effect and the absence of surrounding edema made a brain tumor or abscess unlikely, and suggested the possibility of multiple demyelinating lesions. Subsequent course with clinical recovery and an improving CT scan confirmed the diagnosis.

The Modified Ophthalmological Examination (fluorescein angiograpy, indirect ophthalmoscopy with scleral identation)

Somewhat more esoteric is the careful examination of the eyes for the occurrence of phenomena which have been found to be associated with MS. In 1944, Rucker[10] reported that he had observed an opacity that surrounded segments of the retinal veins of some patients. He subsequently followed these patients and 62% of them developed MS. Over the years he examined 1,100 MS patients and noted that 10% of them had this sheathing of the retinal veins.[11]

We recently described the methods[12] which are routinely used at the Health Sciences Center MS clinic to study perivenous sheathing. Perivenous sheathing is often subtle, and when this is the case, we use steroscopic fundus photographs so that we may carefully examine the retina as extensively as possible. Fluorescein is then injected intravenously, and it stains the area of perivenous sheathing. The areas of staining are photographed to document their correlation with the suspicious areas seen on fundus photography.

We reported an association between perivenous sheathing the the progressive course of MS.[12]

Since perivenous sheathing may be indentified on a routine ophthalmological examination, and may be the first manifestation of the development of multiple sclerosis, it is worthwhile to keep this association in mind. A diagnosis of multiple sclerosis should, however, not be made on the basis of this manifestation alone, but in the presence of other neurolgic signs, and the absence of aphthous oral or genital ulcers, it should be considered of high likelihood.

We believe that there is a form of uveitis, which is unique to and a mainfestation of multipe sclerosis.[12] However, it occurs in only 2.4% of MS patients. It affects

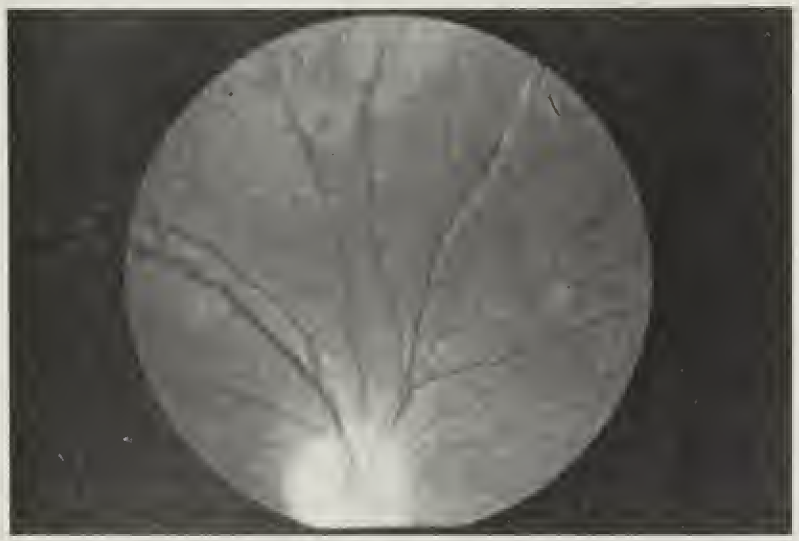


Figure 8
Case 6. Perivenous sheathing of the superior nasal retinal vein (1 o'clock).

the inferior pars plana of the uveal tract most severely and the severity of its presentation may vary from an acute flare up mimicking an iridocyclitis or pars planitis, to an indolent or subclinical state.

When in this latter state, a routine ophthalmological examination will fail to reveal it. However, the pars plana can be visualzied by widely dilating the pupil, and indenting the sclera overlying the inferior pars plana which is brought into view.

The uveitis may present clinically prior to the onset of MS, as occurred in the following patient.

Case 6: A 20 year old female developed blurred vision of the left eye at the age of 9. Cells were seen in the anterior vitreous and an exudate was noted to overlie the retina inferior to the macula. She was treated with systemic and topical steroids. Six months later exudate was seen to overlie the ora serrata and pars plana of the right eye. A cataract had developed on the left. At the age of 14 the patient developed pain and swelling of the fingers of both hands, this spread to involved the joints of all 4 extremities. The symptoms would recur acutely and last up to a week. This was seen to be accompanied by mild diffuse swelling and tenderness. She was diagnosed at that time as having possible juvenile rheumatoid arthritis. At 15 she developed vertigo, vomiting and gross vertical nystagmus, and 2 days later awoke with loss of vision of the right eye, a central scotoma and visual acuity of 20/200, which failed to improve. When 16 she complained of L'hermitte's phenomenon (electrical shock sensation) which radiated to the left arm. At 17 she developed numb feet, and a few months later a recurrence of vertigo; and an episode of left arm numbness, six months later she developed right hemibody numbness. These improved over time. At 18 she complained of a burning sensation affecting the right leg initially, and then involving the left leg. The burning has perisisted for the last 2 years. At 19 the patient had a visual acuity of 20/25 on the left, and 20/400 on the right. Her strength was normal, but hyperreflexia of the lower extremities and bilater Babinski reflexes were noted. Sensation an coordination were normal. Ocular examination of th time revealed perivenous sheathing affecting both eye (Figure 8) and small white exudates over the inferi pars plana on the right. The pars plana on the left coul not be visualized.

Another case is of interest because although th patient does not have multiple sclerosis yet, she has family history of MS, and some of the ocula manifestations of the MS-specific form of uveitis. W are very concerned that she may one day develop MS

Case 7: A 22 year old female had noted floaters and ligh flashes in the left eye two months previously. Slit-lam biomicroscopy of the left eye showed retrolenticula cells, minimal edema of the fundus and several sma vitreous puff balls. She has had no neurologi symptoms, and the family declined a neurologi examination at this time, becaue they did not wish t unduly alarm the patient about the possibility of he developing MS.

Comment: The value of having the potential t diagnose multiple sclerosis before it clinically expresse itself, will be maximal when a cure for MS become available. Until such a time the early diagnosis of MS i of doubtful benefit to a patient who is not disabled. A accurate diagnosis in more severely affected patient will remove doubts and obviate the need for repeate expensive neurological consultations and procedures.

Acknowledgement

Our thanks to Richard Wachter, M.D. and Pete Christenson, M.D. for their assistance in providing th demonstrated CT scans.

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Biliary Tract Imaging With Radionuclides:

New Life for an Old Procedure

Robert E. Henry, M.D.
Michael J. Daly, M.D.

Abstract

Imaging of the liver, gall bladder and biliary tract with Tc-99m labeled biliary agents is useful in the assessment of patients with suspected acute cholecystitis. This procedure should replace intravenous cholangiography in most institutions. Cholescintigraphy is useful in the evaluation of patients with jaundice, particularly in situations where percutaneous transhepatic cholangiography is not available or is contraindicated. Cholescintigraphy also has a role in the evaluation of the jaundiced neonate where biliary atresia is considered. This procedure may also be used to augment conventional liver scanning when an intrahepatic gall bladder or distended biliary ducts are suspected to be the cause of a focal lesion.

Imaging of the gall bladder and biliary tract is an important tool in the evaluation of jaundice and biliary tract disease. At the present time a variety of procedures are available to image these structures, each with its own unique advantages and limitations. The purpose of this report is to describe one of these techniques, radioisotope cholescintigraphy, in some detail and to correlate its use with other diagnostic procedures.

Rose Bengal I-131 has been available for over 20 years for the evaluation of liver function and for the diagnosis of biliary tract obstruction. Biliary tract imaging with Rose Bengal I-131, however, has not been in great demand for several reasons. The physical characteristics of the I-131 gamma photon are not optimal for imaging with the gamma camera. Rose Bengal is rapidly excreted from the biliary tract into the bowel, and the residence time in the colon is relatively long, resulting in a relatively high radiation dose to the colonic, mucosa thus limiting the dose that can be administered. The net result of suboptimal characteristics and insufficient gamma photons is poor quality, low resolution images. Because of these limitations, Rose Bengal I-131 has been used mainly to document complete obstruction of the biliary tract when other tests could not be used. Recently, several radiopharmaceuticals have been introduced which couple Tc-99m, which has excellent physical characteristics for imaging, with compounds which are excreted through the biliary tract. The most promising is the iminodiacetic acid (IDA) family of drugs.[1] These radiopharmaceuticals are easily prepared from commercial kits and are ready for immediate use. Following IV Injection they are cleared rapidly from the blood and accumulate in the hepatocytes of the liver. Shortly thereafter they are excreted into the bile ducts,

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From: Univ. of Arizona Health Sciences Center, Dept. of Radiology Tucson, AZ 85724, and Veterans Administration Medical Center, Nuclear Medicine Service, Tucson, AZ 85723

accumulate in the gall bladder and empty into the small bowel. Thus, cholescintigraphy with this group of radiotracers allows rapid evaluation of hepatic function, gall bladder function and patency of the biliary tract. Like other radiopharmaceuticals in common use, the IDA drugs do not produce a pharmacologic effect in the patient and no toxic or allergic reactions have been reported with their use.

It should be recognized that the radiotracer procedure demonstrates the functional integrity of the hepatobiliary system, whereas ultrasound, CT scanning and transhepatic cholangiography demonstrate the morphologic anatomy of these structures. Moreover, because of the resolution of the detection instruments and other technical factors, imaging of the gall bladder with radionuclides is not appropriate for detection of gall stones. Oral cholecystography or ultrasound should be used for this purpose.

Biliary Tract Imaging with PIPIDA

During the past year we had the opportunity to evaluate the efficacy of Tc-99m p-isopropylacetanilido-iminodiacetic acid (PIPIDA, Diagnostic Isotopes, Inc., Bloomfield, N.J.), one of the IDA family of biliary tract imaging agents, in a variety of patients with liver and biliary tract disease.

Following a fast of three hours or more the patients were administered 5mCi of Tc-99m PIPIDA intravenously. The gamma camera detector was placed over the patient's abdomen to include the heart, liver, duodenum and jejunum. Static images were made at 15 minute intervals for one hour. If gall bladder or bowel activity was not detected by 60 minutes, additional images were obtained at 2 and 6 hours following injection. If intestinal activity was still not apparent, additional views were made at 18 to 24 hours. In most of the patients, the information detected by the gamma camera during the first hour after administration of PIPIDA was also recorded into computer memory for analysis of the kinetics of PIPIDA accumulation and excretion. Aside from the venipuncture, the procedure was noninvasive and the personal attention of a radiologist or other physician during the procedure was not required.

A normal biliary tract study obtained with Tc-99m PIPIDA is shown in Figure 1. The radiopharmaceutical clears rapidly from the blood pool and analysis of time activity curves generated by the computer indicated that in normal patients more than 90% of the PIPIDA had cleared from the blood within three to four minutes after injection. In normal patients the activity accumulates rapidly in the liver, whereas, if hepatocellular disease is present, slow clearance from the blood and slow accumulation in the liver can be expected. In normal patients, activity in the common bile duct and gall bladder apppears within 15 to 30 minutes postinjection. The activity in the gall bladder continues to increase for 2 to 3 hours. Between 30 and 45 minutes activity is seen within the duodenum. At 24 hours activity will be limited to the colon. In addition to liver, gall bladder, biliary tract and bowel activity, small amounts of tracer may appear in the kidneys. The amount of renal activity is usually small and does not interfere with interpretation. The amount of renal activity may be inversely related to the degree of protein binding of the radiopharmaceutical.[1]

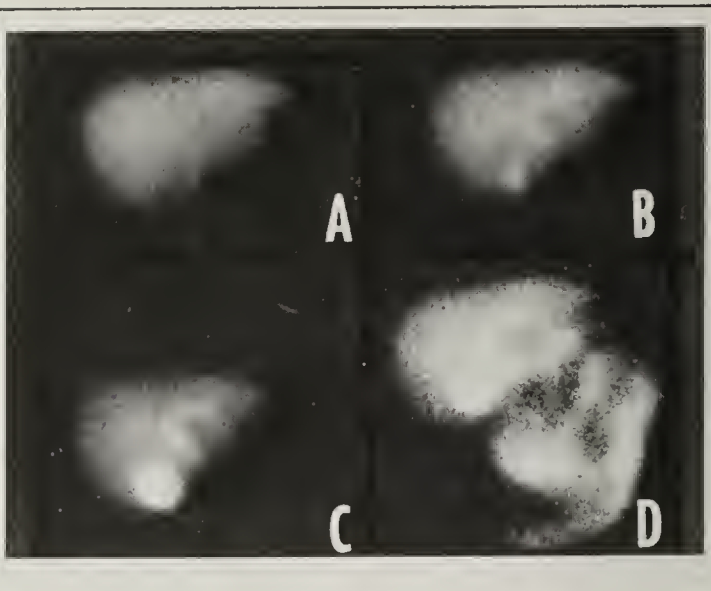

Figure 1
Normal biliary kinetic study using 99mTc-PIPIDA. Five min after injection the liver is seen on the anterior view (A). Minimal cardiac and background activity is present indicating good hepatic function. The inferior edge of the right lobe has a circular defect. By 15 min (B) intrahepatic bile duct and gall bladder activity is visualized. At 30 min it is apparent that the "defect" seen on the earlier image is the gall bladder. Patency of the common bile duct is confirmed on the 60 min image (D) which shows duodenal and small bowel activity.

Evaluation of Right Upper Quadrant Pain

One of the most useful applications of biliary tract imaging with radioisotopes is evaluation of the patient with right upper quadrant pain in whom acute cholecystitis is suspected. In acute cholecystitis the cystic duct is obstructed by stones or inflammation and the gall bladder will not visualize by various radiographic or radionuclide techniques. In this clinical setting, however, oral cholecystography is not expedient because of the overnight preparation and frequent failure to absorb the cholectystopaque tablets. Intravenous cholangiography has been used to evaluate patency of the cystic duct in patients with suspected acute cholecystitis.

Intravenous cholangiography, however, is associated with an undesirably high rate of contrast reactions: one in 700 examinations will require therapeutic intervention and death occurs once in 5000 examinations.[2] It is understandable that radiologists have been anxious to substitute a less hazardous procedure. In our experience and that reported in the literature[3] [4] evaluation of patients with suspected cholecystitis with IDA drugs has been quite successful. As demonstrated by figure 2, a patient with acute cholecystitis and normal liver function will rapidly accumulate the radiopharmaceutical in the liver and excrete it into the common duct and duodenum but the gall bladder does not visualize. Visualization of the gall

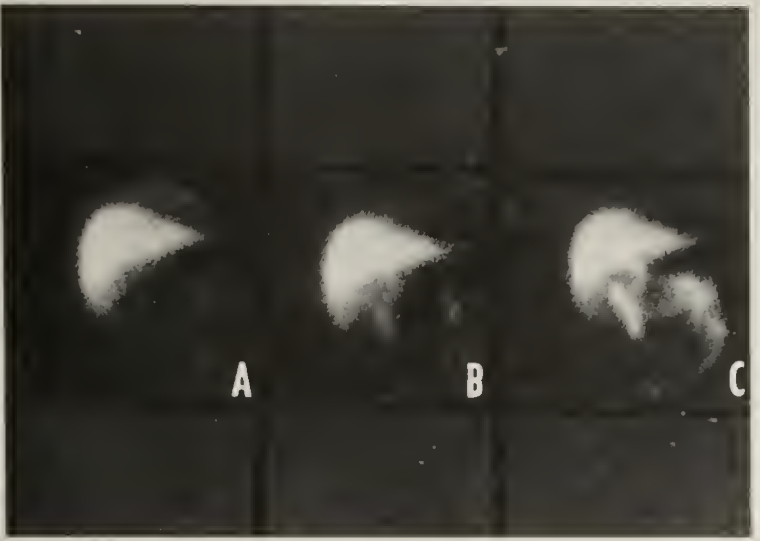

Figure 2
Acute cholecystitis: Five (A), 30 (B) and 60 (C) min after Tc-99m PIPIDA injection, normal liver, common bile duct and intestinal activity is seen indicating good hepatic function and patent bile ducts. The gall bladder did not visualize. At surgery the patient had acute cholecystitis and a stone in the cystic duct.

bladder, therefore, excludes acute cholecystitis or cystic duct obstruction. A non-functioning, non-visualized gall bladder may also occur in some patients with chronic cholecystitis or pancreatitis. It has been suggested that patients with non-visualization of the gall bladder due to chronic cholecystitis can be differentiated by mmediately re-examining the patient following cholecystokinin administration and a second dose of the biliary imaging radiopharmaceutical.[3] Visualization of the gall bladder on the repeat study indicates patency of the cystic duct and is consistent with chronic cholecystitis. Reports in the literature indicate that with the use of cholescintigraphy in the diagnosis of acute cholecystitis, the true negative rate approaches 100% and the true postivie rate is approximately 95% with an overall accuracy of 98%.[4]

Evaluation of the Patient with Jaundice

In the evaluation of jaundice one must determine whether it is due to hepatocellular disease or obstruction. If obstruction is detected the location and cause must be determined. In the jaundiced patient, visualization of the duct or gall bladder is unlikely with either intravenous or orally administered cholecystopaque if the serum bilirubin is greater than 3 mg percent. Sonography, if available, is probably the procedure of choice for the initial examination of the aundiced patient. CT Scanning of the abdomen may also be used but is more expensive and exposes the patient to onizing radiation. If dilated bile ducts are observed by either of these two procedures, percutaneous transhepatic cholangiography (PTC) with a Chiba Needle will demonstrate, in most instances, the exact ocation and, at times, the nature of the obstruction.[5] Although the complication rate using the Chiba needle is ess the 3%, it requires an experienced radiologist. PTC cannot be performed in an uncooperative patient, and ascites, bleeding tendency, severe anemia, and infection are contraindications to its perfomance. An alternate procedure to PTC is endoscopic retrograde cholangiopancreatography (ERCP). In 75% of patients with biliary obstruction it will reliably demonstrate the nature and level of obstruction. ERCP, however, is technically difficult, quite uncomfortable for the patient and is not widely available.

Imaging of the biliary tract with Tc-99m PIPIDA or similar radiotracers is possible despite significant elevation of serum bilirubin. In our series, 92% of patients with serum bilirubin 2.5 mg percent had liver and biliary tract images graded as good or excellent. Good visualization of the liver, gall bladder, common bile duct and gut allowed exclusion of extra-hepatic obstruction in a patient with Laennec's cirrhosis and a serum bilirubin of 20 mg percent (Figure 3).

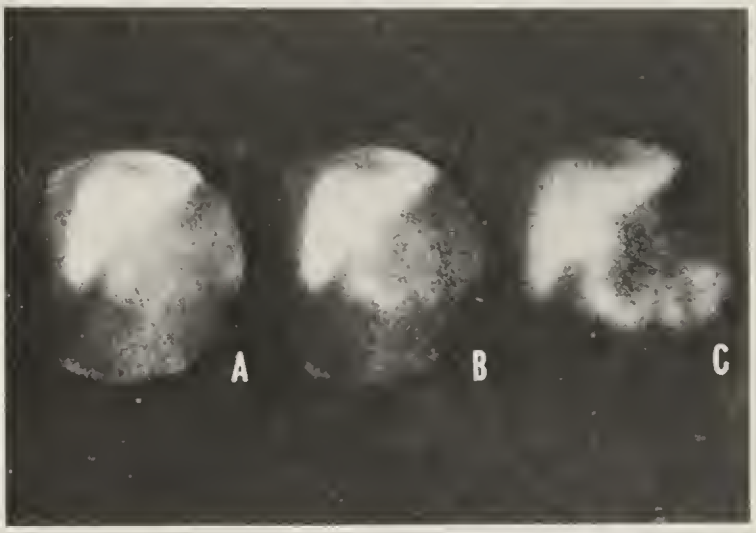

Figure 3
Hepatocellular Disease: Because of a serum bilirubin of 20 mg percent, extrahepatic obstruction had to be excluded in this patient with cirrhosis. Poor hepatic function is manifested by prolonged cardiac blood pool activity (above the left lobe of the liver) and renal activity. By 30 min (B), however, activity is present in the common duct and gall bladder. At 60 min (C) activity is in the gut excluding extrahepatic obstruction as the cause of the jaundice.

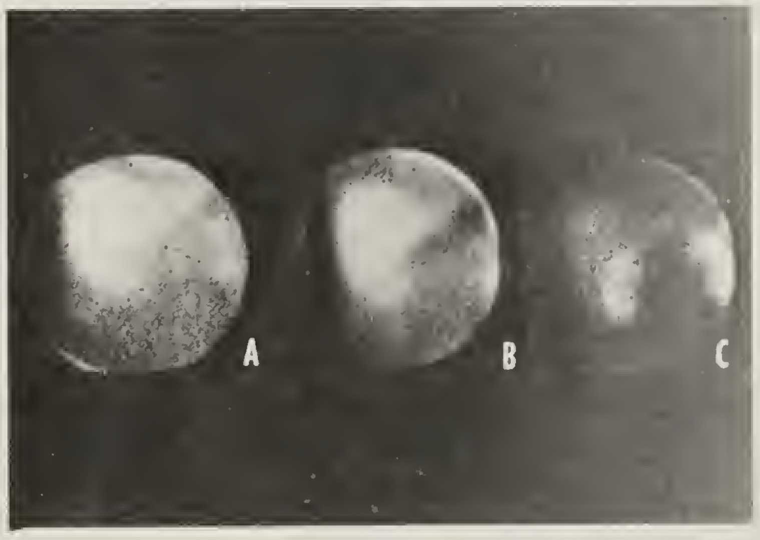

Figure 4
Complete Extrahepatic Obstruction: Jaundice appeared in this patient who had previous surgery for carcinoma of the gall bladder. At one (A), two (B) and 24 hours after Tc-99m PIPIDA administration, hepatic activity is seen but no activity appears in the common duct or bowel. Renal activity is prominent, particularly at 24 hours (C), because the kidney is an alternate source of excretion for this tracer. A transhepatic cholangiogram documented obstruction of the hepatic duct at its exit from the liver.

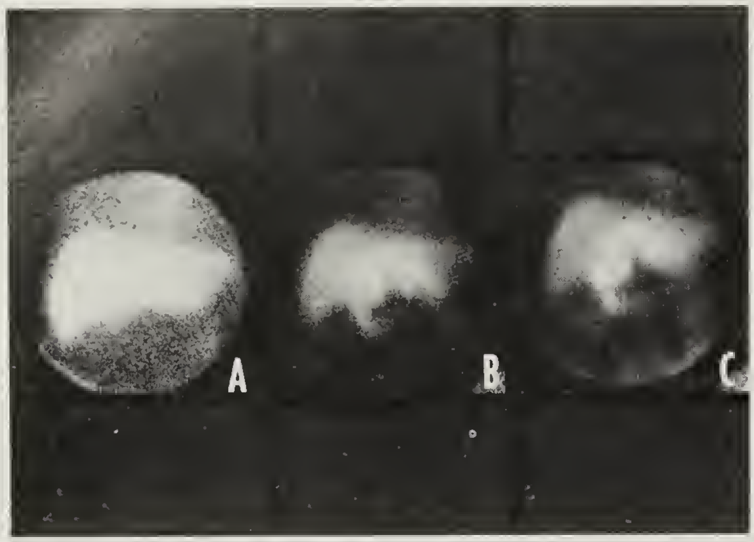

Figure 5
Incomplete Common Duct Obstruction: In this patient with a stricture of the common duct following cholecystectomy and common duct exploration, hepatic clearance is slower than normal as shown by increased cardiac and renal activity at 15 min (A). At 45min (B), the common duct and intrahepatic ducts show increased activity but only a small amount of tracer has entered the gut by 90 min (C) indicating partial obstruction of the common duct. The stricture was documented by ERCP.

Imaging with IDA radiopharmaceuticals in partial or complete obstrution will usually allow the site of obstruction to be detected. Because of the inherent resolution limitations of gamma camera systems, however, the nature of the obstruciton cannot be determined. The diagnosis of complete obstruction by this technique is relatively straightforward. Depending on the duration of the obstruction and the consequent impairment of hepatocellular function, hepatic uptake of the tracer will be normal or moderately delayed. Although activity may be seen within the common bile duct, delayed images obtained at intervals up to 24 hours after injection will demonstrate failure of the tracer to appear in the intestine (Figure 4). In contrast, patients with severe hepatocellular disease have a prolonged duration of hepatic tracer accumulation and excrete at least some of the tracer into the bowel within 24 hours. Some patients with severe hepatocellular disease may be difficult to distinguish from patients with partial obstruction. When appearance of activity in the intestine is delayed for several hours or more one can make the diagnosis of incomplete obstruction with confidence if hepatic uptake is normal and a distended common bile duct is observed (Figure 5). When the hepatic uptake of the radiopharmaceutical is slow, the common bile duct is not seen or is not dilated, and the tracer appears in the intestine after several hours, the most likely diagnosis is hepatocellular disease. Unless images of the common duct area are obtained at regular intervals until bowel activity appears, incomplete obstruction cannot be entirely excluded. Computer assisted analysis of the kinetics of the radiotracer accumulation and excretion from the liver may prove to be of assistance in distinguishing patients with hepatocellular disease from those with incomplete extrahepatic obstruction.

A difficult diagnostic problem is the differentiation of neonatal hepatitis from biliary atresia. This differentiation is important because infants with biliary tract atresia may be aided by the Kasai procedure. Transhepatic cholangiography is usually not successful in making this differentiation because of the rudimentary intraphepatic biliary radicals and ERCP is technically unfeasible in infants. Visualizaiton of gut activity 24 to 48 hours following the administration of Tc-99m PIPIDA or a similar radiopharmaceutical, indicates that neonatal hepatitis is the cause of the jaundice. Unfortunately, some infants with severe cholestasis due to hepatitis will not excrete the tracer and surgical exploration and intra-operative cholangiography will be necessary to differentiate the two disorders.

Biliary Tract Imaging as a Supplement to Liver Scanning

A particularly useful application of biliary tract imaging with Tc-99m labeled biliary agents is evaluation of focal liver abnormalities seen on routine liver scanning. A defect in the inferior margin of the right lobe of the liver due to a prominent gall bladder fossa or intrahepatic gall bladder can be differentiated from tumor or other focal lesions by cholescintigraphy (Figure 1). A "Y" defect or prominent portahepatis caused by distended biliary radicals due to obstruction may also be demonstrated with PIPIDA.

Other Applications

Tc-99m PIPIDA and similar agents appear particularly useful in postoperative evaluation of biliary-enteric shunts and in patients who develop signs of biliary obstruction following common duct exploration. Ultrasound may not be successful in these patients because of gas in the shunts or ducts and because bile duct dilatation may have been present preoperatively. Cholescintigraphy may also be used to demonstrate bile leaks after surgical or blunt trauma. A relatively unexplored area is the measurement of gall bladder contractility with sinclaide, a synthetic analogue of cholecystokinin. This may have potential application in the evaluation of patients with unexplained right upper quadrant pain and fatty food intolerance without demonstration of gall bladder disease by conventional methods; the so-called biliary dyskinesia syndrome.

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The Current Use of Vitrectomy nstrumentation in Ophthalmology

James D. Kingham, M.D.

In the few short years since Machemer[1] in 1971 described vitrectomy through the pars plana with his Vitreous Infusion Suction Cutter, there has been a plethora of vitrectomy instrumentation introduced. With improved instrumentation and expertise the ndications for ocular surgery with these instruments have grown rapidly and are no longer confined to the vitreous body. Indeed, their use in anterior segment surgery has augmented or made obsolete older, established techniques.

Instrumentation

All vitrectomy instrumentation has of necessity, 3 parameters in common.

1. viteous is cut
2. vitreous is evacuated from the eye
3. vitreous is replaced by a balanced salt infusion

Thus, the name for Machemer's original instrument; Vitreous Infusion Suction Cutter (VISC). In addition, a sophisticated array of intraocular fiber optic light pipes has replaced coaxial external illumination.

The cutting tip, which is introduced into the eye at the corneoscleral limbus, or more posteriorly through the pars plana, is about 40 mm long and about 1.5 mm in diameter. It consists of a hollow tube with a cutting port near the end, and a concentric inner tube which rotates or oscillates as vitreous is drawn by suction into the cutting port. Infusion is provided through a small aperature in the outer tube with the VISC, or infusion may enter the eye through a needle or cannula at a remote site in the eye as with the Ocutome.[2] Over the entire suction, cutting, infusion device can be added a fiber optic light pipe for work deep in the eye, which brings the total diameter of the instrument to 2.41 mm. A separate fiber optic light may be introduced remotely, as with the Ocutome, allowing the outside diameter of the cutting tip to remain small (Ocutome 0.89 mm, VISC 1.63 mm).

The surgery is usually performed under visualization with the operating microscope but in certain difficult situations indirect ophthalmoscopy is used.

Entrance into the eye may be affected via the anterior approach at the corneoscleral limbus, or posteriorly through the pars plana. The anterior approach is used for anterior surgical problems such as blood or vitreous in the anterior chamber, pupillary membranes, and cataract. The posterior approach is used for problems deep in the vitreous and on the surface of the retina. Pupillary membranes and cataracts can also be removed by the pars plana approach.

From: Univ. of Arizona Health Sciences Center, Dept. of Ophthalmology, Tucson, AZ 85724

Table I
Indications for surgery
Via anterior approach

1. Cataracts
   a) congenital
   b) secondary
   c) traumatic
2. Management of vitreous loss
   a) cataract extraction
   b) keratoplasty
3. Removal of hyphema
4. Membranectomy
   a) post surgical
   b) post trauma
5. Anterior segment reconstruction
6. Vitreocorneal adhesion
7. Acute trauma

Indications for Vitrectomy Surgery Via the Anterior Approach
Table 1

Cataracts in young people are difficult problems because of a dense adhesion between the posterior lens capsule and the anterior vitreous face. Congenital, traumatic, and secondary cataracts from uveitis lend themselves well to removal by vitrectomy instrumentation. The lens capsule, cortex, and nucleus can all be removed via a 2 mm incision with minimal operative or post operative morbidity.[3,4]

Vitreo-corneal touch. Vitreous loss during cataract extraction is a serious complication that can lead to imperfect wound closure, retinal detachment, and cystoid macular edema. Vitreous touch to the cornea during corneal transplant can cause graft failure. Proper management of vitreous by anterior vitrectomy in these cases will frequently abort or ameliorate the complications.[5] Vitreous incarcerated in a cataract wound can be removed as a secondary procedure.

Hyphema. Recurrent bleeding into the anterior chamber following blunt trauma leads to acute glaucoma and blood staining of the cornea. Clotted blood is difficult to remove by conventional means, but is easily removed via a small incision with the VISC or Ocutome. Recurrent hemorrhage is unusual and results are good.

Pupillary membranes as a result of trauma or proliferation of tissue after extracapsular cataract extraction, can be removed by the anterior or posterior approach.[6] The anterior approach is sometimes safer if the surgeon has no idea of the ocular status behind the pupillary membrane. Puplis that have been occluded for 25 years or more have been opened with good visual results.

Indication for Vitrectomy Via The Posterior Approach
Table 2

Vitrectomy via the pars plana is performed whenever it is necessary to remove the majority of the vitreous body because it is either opaque or diseased. Long standing vitreous hemorrhage previously not amenable to surgical removal is the paradigm of indication for vitrectomy.[7] Vitreous hemorrhage occurs as a result of such diverse disease states as diabetic retinopathy, sickle cell SC disease, venous occlusion and others. Amyloidosis,[8] reticulum cell sarcoma,[9] chronic posterior uveitis,[4] and parasitic infestation of vitreous[10] all cause blinding vitreous opacities, and all are amenable to removal by vitrectomy.

Table 2
Indications for surgery via
posterior approach

1. Vitreous Opacity
   a) hemorrhage
   b) uveitis
   c) amyloidosis
   d) reticulum cell sarcoma
2. Vitreoretinal traction syndrome
   a) traction retinal detachment
   b) rhegmatogenous retinal detachment
   c) giant retinal tears
   d) epiretinal membranes
   e) massive vitreous retraction (MVR)
3. Lens removal
   a) cataract (all types)
   b) lens lost in vitreous
   c) persistent hyperplastic primary vitreous (PHPV)
4. Pupillary membranectomy
   a) traumatic
   b) post surgical
   c) after IOL implantations
5. Bacterial or fungal endophthalmitis
6. intraocular foreign body removal
7. Malignant glaucoma
8. Intravitreal parasites
9. Acute trauma

Management by vitrectomy of fulminating bacterial or fungal endophthalmitis is both diagnostic and therapeutic.[11] The aspirate is examined microscopically and cultured. The removal of the infected vitreous is analogous to draining an abcess. When combined with intravitreal injection of antibiotics and steroids, useful vision can return to eyes which otherwise surely would have been lost to the infection.

Removal of traction bands in the vitreous augments retinal reattachment surgery in difficult cases.[12] Traction retinal detachment as a complication of proliferative retinopathies (diabetes, sickle cell SC, retrolental fibroplasia) is managed by severing the vitreoretinal traction bands.[7]

Irritative nonmagnetic intraocular foreign bodies with vitreous hemorrhage are removed by first clearing the opaque media with vitrectomy.[13] When the foreign body is found it is removed with intravitreal foreign body forceps.

Acute and sub-acute trauma is managed by removal of damaged lens material and bloody vitreous, and definitive repair of detached retina, when necessary.[14]

Complications of Vitrectomy

Complications may be related to surgical technique and should be avoidable, or they may be related to the underlying disease and as such are not avoidable.[15] Long surgical procedures via the pars plana result in cloudy corneas and lenses, presumably because of a less than ideal infusion solution, or because of mechanical trauma, or both. Diabetics have a higher incidence of post operative corneal and lens cloudiness than do non diabetics. Iatrogenic detachment of the retina is frequently encountered as a result of retinal traction and hole formation, or hole formation with the vitrectomy instrument. Post operative rubeosis iridis and subsequent glaucoma may be expected in 10-50% of all diabetic eyes undergoing vitrectomy. Endophthalmitis after vitrectomy is rare.

Summary

The development of vitrectomy instrumentation has greatly augmented the armamentarium of surgical approaches to ocular disease. It is useful in any condition which imparts an opacity to any of the intraocular structures such as the anterior chamber, lens, or vitreous. It is useful in the management of acute and old trauma, and in any condition in which vitreous traction is implicated. It is difficult and exacting microsurgical technique with a propensity for intraoperative iatrogenic complications. It must be stressed that this surgical technique must be used only by those surgeons who are prepared to handle the complications.

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Evaluation of Hearing Loss in Children

Charles F. Koopmann, M.D., Jr., M.D.
Stanley W. Coulthard, M.D.

Until relatively recently, persons born with severe hearing impairments were raised in almost total isolation, considered "deaf and dumb," and were not prepared for active participation in the hearing world. They tended to segregate with other deaf persons, communicating by sign language. It was only within the last century that dedicated professionals made serious attempts to teach lip reading and oral communicaton. Now, with advances in audiological equipment, hearing aid technology, and the awareness of health care practitioners of the devastating effects of failure of diagnosis, many children whose hearing loss is detected before the age of two can learn to speak adequately.

Before discussion of detection of high risk children we should attempt to review degrees of hearing impairment (and their functional sequelae) and sites of lesions. Table I shows the relationship between hearing level (in decibels) and probable handicaps. One basis for classification of hearing impairment is the time of onset - i.e., congenital or acquired. Congenital losses are present at birth and may, or may not, be the result of hereditary factors. The functional results of acquired hearing loss may be the same as a congenital problem of like magnitude if it occurs before speech and language have developed.

From: Univ. of Arizona Health Sciences Center, Depart. of Surgery, Division of Otolaryngology, Tucson, AZ 85724.

The site of the lesion may be conductive (from external auditory meatus to the footplate of the stapes), sensorineural (either cochlea or cochlear nerve), or central nervous system. Conductive hearing losses result from sound waves not being transmitted to the cochlea. Most conductive losses are treatable by medical or surgical intervention, although hearing aids are useful if there is some contra-indication to surgical intervention. In general, sensorineural losses are not correctable and thus, early recognition and amplification is essential. Children with central lesions may have normal hearing sensitivity to pure tones (if they can be conditioned to respond) but are delayed in speech and language development.

Delay in or failure to diagnose hearing losses in infants has profound social and economic consequences. Mencher has estimated that it costs $10,000 in rehabilitation for each year's delay in detection. More important socially is the extreme handicap in interpersonal relationships. A deaf 2 year old has no useful verbal language and at 5 has only a speaking vocabulary of 200 words while a 5 year old child with normal hearing has between 5000 and 26,000 words. Thus, identification of the hearing impaired child in the first year of life is essential for adequate intellectual development.

We now arrive at the problem of identification of these persons. In an attempt to manage this problem a Joint Committee on Newborn Hearing Screening was established by the American Academy of Ophthalmology and Otolaryngology, the American Academy of Pediatrics, and the American Speech and Hearing Association. They felt that 5 questions were important in high risk patients:

1. Is there a family history of hearing impairment?
2. Did an intrauterine fetal infection occur - rubella, cytomegalovirus, herpes, syphilis?
3. Are there congenital anomalies of the face or skull - malformed, low-set, or absent pinnae, cleft palate?
4. Was there a birth weight below 1500 grams?
5. Was the infant's serum bilirubin elevated?

Feinmesser and Tell[3] added:

6. Was there neonatal hypoxia?
7. Was there neonatal sepsis?

Consequently, a gestational, perinatal, and postnatal history is important. Physical examination may reveal a cleft palate or other craniofacial anomaly (60 to 90 percent of these infants have decreased hearing), Waardenburg's Syndrome (hypertelorism, heterochromia, white forelock), albinism, trisomies, cerebral palsy, congenital syphilis, or cardiac lesions (including Jervell Lange-Nielsen), malformation of the pinna, external auditory canal, or extremities. Laboratory tests should be based upon the history and/or physical examination and may include viral cultures and serological examination early in life and thyroid function (Pendred's Syndrome) and an EKG (Jervell Lange-Nielson Syndrome) later. Pneumatic otoscopy is optimal but is very difficult in the neonate and will only identify tympanic membrane problems or middle ear effusions but will give no data on cochlear function.

Table 1

Hearing Level (dB) 1969 ANSI	Interpretation	Degree of Handicap
0 - 25 dB	Normal	No significant educational difficulty
25 - 40 dB	Mild Loss	Difficulty with faint speech; benefits from preferential seating and amplification
41 -55 dB	Moderate Loss	Difficulty with conversation speech; needs preferential seating, amplification auditory training, and special education classes.
56 - 70 dB	Moderately Severe Loss	Same as above
71 - 90 dB	Severe Loss	Hears only loud voices; may understand vowels but not consonants; needs amplification, special seating; special education, speech and language classes
91 dB or greater	Profound Loss	Hears only few loud loud sounds; cannot rely on hearing as source of communication

Adapted from Davis H, and Silverman D: Hearing and Deafness, 3rd Ed., Holt, Rinehart, and Winston, New York, 1970; and Goodman, A.C., Reference zero levels for pure-tone audiometers, Maico Audiological Series, Vol. 4, Rept. 7, 1966.

Mencher retrospectively found that items 1-5 would have correctly indentified two-thirds of the children.[4] Feinmesser and Tell compared the High-Risk Registry with behavioral evaluation, and found that the Seven Item Registry located 17 of 23 children where only 6 of the 23 would have been found with behavioral criteria.[3] Thus, the Joint Committee in 1974 recommended: "Infants falling in this (high risk) category should be referred for an indepth audiolgical evaluation within two months after discharge from the nursery."[5]

If one combines behavioral screening and high risk registry, 80 percent of the children can be identified properly by age 2.[6] In practice, when applying these criteria, 6 to 8 percent of the general newborn population would fall into the group requiring audiological studies and of this group to be tested 2 to 4 percent would prove to have a hearing loss.

Behavioral screening utilizes a carefully calibrated sound stimulus; an infant arousal response of two motor responses to the stimulus during a fixed observation nterval following the presentation of the sound; and observations by two observers. The recommended procedure as outlined by the Nova Scotia Conference is as follows:

1. The stimulus should be 90 dB sound pressure evel; duration of 0.5 - 2.0 seconds; inter-test interval minimum of 15 seconds; random noise with a low frequency attenuation of 30 dB or more per octave below 750 Hz.
2. The pretest behavior state of the infant must be described carefully; preferably the child should be asleep with eyes closed and no body movement for 15 seconds before the test sound.
3. The only acceptable response is a generalized body movement involving more than one limb and accompanied by some eye movement.
4. Scoring is done by two observers independently.

This test method fails to identify children with hearing osses less than 75 dB and thus should be combined with the registry.

The crib-o-gram has been proposed as an alternative to behavioral screening or testing by Simmons.[7] He feels that advantgages of the crib-o-gram include 1) lower cost, 2) the machinery can take several repeated observations at various times, 3) is likely to be more independent of nursery routines and random responses, 4) can be performed around the clock.

This method utilizes a motion sensitive transducer attached underneath the infants's bassinets with a strip chart to record motion, an automatic timer, and a loudspeaker. A high frequency sound introduced at scheduled intervals and the infant's responses are recorded. Simmons reports a general incidence of finding 2.5 severe hearing losses per 1000 births and an incidence of 14 per 1000 in the ICU population. This method may undergo general implementation within the next few years.

In the office setting one method of screening entails the use of noisemakers. Downs recommends five: two with high frequency sounds (a bell and a high pitched rattle sound), two with low frequency sounds (a squeeze toy and a clacker), and one loud sound (bell or rattle) covering most of the frequency range.[8] The child is distracted using toys and the test sound is made outside his peripheral vision. One can expect the following responses based upon the child's age:

1. Birth to 4 months: reflex movements such as eye blink or startle.
2. 4 - 7 months: turning the head toward the noise.
3. 7 - 9 months: turning the head downward as well as toward the sound.
4. 9 - 13 months: localization in any plane.

This method of evaluation is acceptable in the low risk child but those in the high risk categories deserve more sophisticated methods of screening (as previously described) or as will follow.

Downs feels that tympanometry (impedance testing) with acoustic reflex can be useful in screening infants and children with two limitations:[8] 1) it is of limited value in infants under seven months of age since in this age group its accuracy is only 70% rather than the usual 96% 2) the tympanogram can occasionally be normal in the presence of a cholesteatoma. If a child fails either test, he should be retested within 12 weeks and if he again fails, should be referred for a more complete audiological and otological evaluation.

Respiratory and cardiovascular responses to acoustic stimuli have been evaluated. To date neither are clinically applicable. However, cardiovascular response audiometry has potential advantages over encephalic response (EEG) audiometry in that an intact nervous system is not required. EEG audiometry is excellent in some older infants who fail screening tests. However, in early infancy only 40% of neonates tested reponded to 40 dB SPL and only 85% responded at 50 dB.[9] At present, the variability of its response increases as age decreases and poor results are frequently encountered in patients less than two years of age.

Electrocochleography is a measurement of potentials which arise within the cochlea and the auditory nerve. This may be performed by placing an electrode on the skin of the external auditory canal near the annulus of the tympanic membrane or through the tympanic membrane onto the promontory. It is extremely reliable in measuring the cochlear microphonic and the eight nerve action potential (all peripheral) but does not measure central or brain stem responses. Also, it requires sedation and/or a general anesthetic in the child and, if promontory readings are taken, requires penetration of the tympanic membrane. However, because of its reliability (anesthesia produces no effect on results), electrocochleography should be one of the tools utilized in high risk infants who fail screening testing.

Brain stem evoked response audiometry (hereafter BSER) utilizes surface electrodes to measure potentials which arise in the cochlear nerve and brain stem. One electrode (reference) is placed over the mastoid prominence of the tested ear and the other electrode (active) is placed on the scalp vertex. Events which occur during the first 10 msec following sound stimulation are recorded. BSER has good reliability, is not affected by narcosis or general anesthesia, and is noninvasive. BSER is superior to crib-o-grams because the former method gives information concerning whether amplification is necessary and if so, what the characteristics of the aid should be. BSER offers advantages over electrocochleography in three areas: 1) threshold testing in infants and young children since it requires only surface electrodes and can be performed in a clinic or office, 2) diagnosis of acoustic neuromas, 3) diagnosis of brain stem lesions.

As children reach the age of two to three, play audiometry and pure tone testing become more feasible. Impedance audiometry is easier to perform and is more reliable. Also, in those children who have been diagnosed as having severe sensorineural losses or who may have a congenital middle or inner ear anomaly, radiographic evaluation incorporating polytomography or spiral tomography of the temporal bone is possible. Thus, utilizing data concerning the nature of the impairment (conductive, sensorineural, or mixed) and physical and radiographic findings, one can adequately counsel the parents as to a treatment plan.

Summary

We would recommend that all infants who fall into the seven item high risk group be referred for early otologic and audiologic evaluation *and* follow-up immediately upon their birth or admission to the neonatal intensive care unit. The crib-o-gram would be a worthwhile investment for the neonatal ICU unit for the initial screening, although brain stem audiometry would be the best method of screening the high risk group. Also, all infants who fail to pass behavioral testing should be referred for brain stem audiometry. Electrocochleography should be reserved for patients who have a hearing loss and now need precise threshold measurements. As the child reaches two to three years of age we would then use the more conventional tympanometry, acoustic reflex, and pure tone audiometry if possible.

In conclusion, we would like to stress the early diagnosis of the hearing impaired child so that amplification can begin in the first few months of life. Much of the severe handicap of deafness as it relates to speech and language development can be eliminated if the children are identified and fitted with appropriate hearing aids within the first 12-18 months. Now, with the advances in electrophysiological audiometry, it is now possible to objectively evaluate these infants so that the "deaf and dumb" adult will hopefully become an extinct entity and will be replaced by a productive individual who may indeed have a severe hearing loss but who can still adequately communicate.

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Editorials

Internists:
Is that what we are turning out?

Are the present methods we have for training general internists adequate? As I watch each new batch of third year residents leave the local community teaching hospitals and enter the practice of medicine I wonder whether their training in Phoenix was as good as it could have been and whether it was equal to that which could have been obtained at a university teaching program.

I am concerned that our present medical education system and particularly post-graduate training programs lack significant committment to scientific medical principles. I feel part of this is due to a greater emphasis on the social and psychological aspects of medical care. Although this is an extremely important aspect of medical education, which has been neglected in the past, it presently is given in the same time frame as purely medical information. I believe this may have resulted in short-cutting hard-core medical knowledge upon which future advances in medicine is layered. Futhermore, I wonder whether the local training in the various subspecialty areas is as good as that which can be obtained at a university facility. Although the teachers at the local level are clinicians, the house staff never gets exposure to researchers or faculty persons well-versed in depth in particular areas. I feel that the training we are admistering is rather superficial and practical rather than theoretical. Without the latter, a foundation is lacking upon which building will necessarily need to take place as newer advances in medicine accrue. I have the feeling that we are turning out physicians who will need to be retaught every five years as their structure is lost due to evolutionary changes in medical knowledge. I wonder how often those of us who were taught at university centers, when faced with a difficult diagnostic problem, phone a favored professor at their training university to ask for advice? Where do the locally trained physicians call for help?

I guess what I am saying is that I'm having nostalgic feelings for the old way of doing things. An analogy which seems somewhat appropriate is that between the modern Cadillac that General Motors is producing and the Mercedes-Benz automobile. I seem to see more older Mercedes-Benz' circulating than Cadillacs. Maybe there is something to be said for the old way of doing things.

Marshall B. Block, M.D.
Editor

Arizona Health Sciences Center and the Vice President

On the occasion of this the third year of an issue of *Arizona Medicine* centering on papers from the College of Medicine, it is appropriate to comment on the history of this editorial - early called the Dean's Page. The first such Page was devoted to and penned by the founding Dean, Merlin K. DuVal, M.D. Beginning with that essay and proceeding month after month a review of these pages chronicles the rapid and in many ways, unique success of the College. The review also reveals the influence and accomplishements of Monte DuVal to the benefit of the College, and indeed, medicine in Arizona.

While Dr. DuVal would be the first to admit that the College of Medicine, and indeed the University of Arizona Health Sciences Center, is the result of planning and work by many capable individuals, all recognize the stamp of his strong leadership and thoughtful, farsighted thinking. Whether one looks at the geographical placement of structures or the organization of interrelationships between people working together in this educational enterprise, the evidence of critical and sensitive attention to detail is apparent.

His legacy to Arizona began in 1963. Arriving from the University of Oklahoma School of Medicine, he already had achieved recognition as a Professor of Surgery, Vice Chairman of the Department of Surgery, and Assistant Director of the University of Oklahoma Medical Center. From the perspective of an accomplished administrator, he quickly recruited a few key faculty to begin the task of developing the College from ground zero. Wisely, he began with the Heads of Anatomy and Internal Medicine - Philip Krutzsch, Ph.D. and Oscar Thorup, M.D. These experienced individuals added their expertise in the design of the basic and clinical science areas. Moving rapidly the concept evolved of a health sciences institution which could always react to and move with a changing society in its health care and scientific needs. The campus for the center was placed as close to the main campus of the Unviersity as possible, but yet on land (formerly the University of Arizona polo field) adequate in size for future growth, modification and expansion. Perhaps the key symbolic and functional decision was to build the basic sciences building contiguous to the clinical sciences building and hospital. The basic science educational activities were appropritately placed at the south toward the University Campus and the patient care activities at the north toward Phoenix. The final structure with its functional relationships of library and animal resources in the Basic Sciences Building and the support service, outpatient areas and patient care functions of University Hospital in the Clinical Sciences area has been seen as a model nationally.

The organizational structure was planned and executed in the health sciences complex with equally high quality. The selection of the number and nature of original departments, the faculty promotion and tenure guidelines and the financial plan for clinical faculty salaries, too, have been viewed as models. Medical schools throughout North America visit and question and study Arizona as they attempt to build and remodel their health care enterprises.

Dr. DuVal, endowed with intuitive capacities for design and administration, is recognized throughout the world. Serving on innumerable boards, committees and advisory groups, he has influenced the direction of medicine perhaps as much as any single individual in our society today. National service with the Department of Health, Education and Welfare as Assistant Secretary for Health and Scientific Affairs is seen by many as the pinnacle of this recognition. Closer to home, however, his appointment as Vice President for Health Sciences recognized the culmination of his incredible insight and visions. This administrative decision allowed Monte's influence to impact on all health care teaching and research at the University. The bringing together through his office all disciplines and functions related to health care has allowed those involved in the health sciences to truly function together in educaiton, in research, and in service to the state.

Now the time has come for others to benefit from Dr. DuVal's skills. His resignation from the University of Arizona and appointment as President of the National Center for Health Education mark well his personal recognition that the challenge of the 60's here in Arizona has been met, for he would surely not leave an unstable program or task undone. The papers in the pages of this issue of *Arizona Medicine* attest to the excellence he leaves as a legacy. He can depart in confidence and with pride. Arizona is most grateful! Monte, our hats off to you and our wishes for great success in your new challenge.

Louis J. Kettel, M.D., Dean
College of Medicine
University of Arizona

Auxiliary Highlights

Definitive writing about the hospice concept of caring for the dying patient has increased dramatically in the past five years as the U.S. develops more humanistic concern for the final and limited time span of the terminally ill. The medieval term "hospice" translates from the ancient day way station where travelers could find shelter and comfort from the wearisome journey.

Today's hospice reflects the basis established in England and now spreading across our country as a growing health service to communities. It is natural then for Auxiliary to be involved, as much of the work is done by the volunteer who relates to providing the kind of care offering "relief from distressing symptoms of their disease, the security of a caring environment, sustaining care, and the assurance that they and their families will not be abandoned."

According to James R. Callison, M.D., who wrote for the October 1977 Maricopa *Round-Up*, objectives of the hospice program include helping the patient die at home if he desires instead of in a hospital setting, controlling pain while still allowing the patient to function, and giving supportive encouragement to the families as they asssume responsibilities for the patient's care while he lives and also during the bereavement period. He further notes that the organized hospice program frees up acute hospital beds and reduces hospital and health care costs for the community. The ideal objective inspires: "May you live as long as you want to, and may you want to live as long as you do" in the theory that everyone is a living someone until the moment of death.

Even the professionals among hospice volunteers do not give medical or nursing care. They do not try to change lifestyles in the process of meeting needs and concerns. They do offer emotional support and utilize their initial and ongoing training to evaluate and cope with the unique situations surrounding each death.

Mrs. George T. (Janet) Hoffmann and Mrs. Dennis (Jeanne) Weiland are two Arizona Auxiliary members dedicated to the hospice program. They report a current board of 26 members including nurses, social workers, doctors, lawyer, financial businessmen, funeral director, housewives and ministers.

A full time staff is financed through a grant from HEW, a smaller grant from the Flinn Foundation of Arizona plus other tax deductible assists. Since March first the staff consists of an executive director, nurse practitioner, educator/-

researcher, volunteer coordinator and secretary. The five paid staff members work with approximately sixty volunteers who currently serve more than twenty patients and are also bereavement counseling several families.

The Auxilians profess this to be an exciting group with which to be associated, and indeed the challenge of new concepts emerging into reality offer inspiration in the American tradition. The Valley of the Sun Hospice Association has led the way for other groups even though their primary concern is to perform appropriately in the task at hand.

Happily, this scribe is not in need - today - , but when I stumble upon my "way to go", I hope a hospice volunteer is there to hold the flashlight.

Mrs. Melvin W. (Jean) Phillips
Auxiliary Editor

In Memoriam

Lewis B. Claypool, M.D.

Physician, Patriot and Friend of Man
1916 - 1978

There was nothing equivocal about Lewis Claypool. He was positive, compassionate, and constructive in his private and professional life.

Born in Iowa he was due to graduate from medical school at the University of Iowa in 1941, but he suffered an attack of pneumonia, which left him a severe asthmatic; he came to Arizona seeking relief. (1939) In 1940 he returned to Iowa but lasted only three days and was forced again to return to Phoenix, where he again became employed as an orderly at the old St. Joseph's Hospital. With the onset of WW II he was employed as a chemist in a chemical plant in California. He was refused enlistment by the Armed Forces, and later (as was frequently the case) was drafted and sent to the 4th Infantry. Now he was able to enter the ASTP program and finished medical school at Tulane, and he again returned to St. Joseph's hopsital in Phoenix as an intern in 1947. He was called up during the Korean conflict and served 2 years at Williams Air Force Base and returned to paractice here in Phoenix. Thus began his long romance with the Air Force. He joined the Air National Guard and thereafter gave it loyal service. The Military "the world's largest fraternity" he served with relish.

In the meantime he established a busy family practice with Doctors Carlos Craig and Robert Barfoot, first in the Professional Building and later at 1313 N. 2nd Street in Phoenix.

In later years he was attracted to the professional suites at St. Luke's Hospital and established a solo office there.

Lewis never limited his practice to one hospital. He was a staff member of the five Phoenix hospitals. He was never a drone, and at times served as chief of the medical staff at Memorial and St. Luke's Hospitals and on numerous committees at these and other hopitals in the valley. He was always a booster for organized medicine and served in various capacitites in the County and State Societies.

Here indeed was the compleat physician. Medicine was always a challenge, and he attended his patients with empathy and skill. Military pursuits were also a challenge and enjoyment. He retired with the rank of Brigadier General. Most of all his wife, family and home were his greatest pride and enjoyment.

Professional proficiency, military excellence and family pride, these were the unabashed motives in the life work of Lewis Claypool.

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ArMA Reports

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LEGISLATIVE COMMITTEE

Meeting of the Legislative Committtee of the Arizona Medical Association, held at 810 W. Bethany Home Rd., Phoenix, Arizona, on Saturday, March 3, 1979, convened at 2:06 p.m., Selma E. Targovnick, Chairperson, presiding.

Definition of Terms

It was announced that the definition of terms as adopted during meeting held December 13, 1979, will continue to be used.

H.B. 2124 - Medical Malpractice Insurance

Dr. Sattenspiel updated the committee on the status of H.B. 2124 which would provide for the renewal of the J.U.P. The bill has passed the House with amendments renewing the J.U.P. for two years and providing that the J.U.P. funds would not cover claims arising from the performance of an abortion unless such abortion is necessary to save the life of the woman having the abortion. The Senate Health Committee will be hearing the bill in the near future. INFORMATION ONLY.

S.B. 1247 - Drug Information Center

S. B. 1247 would provide that the Department of Health Services establish a regional poison and drug information center located at and affiliated with the University of Arizona. The center would have a full-time staff including a clinical toxicologist, poison information specialists. specialists and treatment consultants. The bill further provides for the establishment of subregional centers for poison prevention. The Professional Committee and the Board of Directors have reviewed the concept and voiced approval. It was noted that the Senate Health Committee has passed this bill. IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO S.B. 1247.

S.B. 1248 - Health Care Institutions

S.B. 1248 would amend the certificate of need law for health care institutions to conform to the federal law, 93-641, requirements. There was considerable discussion of this bill and it was determined that there are both supportable and opposable elements involved.

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Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence.* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.
Cayey, Puerto Rico 00633

Direct Medical Inquiries to.
MERRELL-NATIONAL LABORATORIES
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215, U.S.A.

Licensor of Merrell®

References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon, R.H., and Leyland, H.M.: A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy. Jan. 20-21, 1977.

Merrell

8-3921 (Y587A)

Whether overweight is a complicating factor... or just uncomplicated overweight.

Tenuate® Dospan® Ⓒ IV

(diethylpropion hydrochloride NF)

75 mg. controlled-release tablets

A useful short-term adjunct in an indicated weight loss program.

Overweight patients in certain diagnostic categories often require strict obesity control. Diethylpropion hydrochloride has been reported useful in obese patients with hypertension, symptomatic cardiovascular disease, or diabetes. While it is not suggested that Tenuate in any way reduces these complications in the overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. (Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.)

In uncomplicated obesity.

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

Clinical effectiveness.

The anorexic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.[1] And the unique chemistry of Tenuate provides "...anorexic potency with minimal overt central nervous system or cardiovascular stimulation."[2] Compared with the amphetamines, diethylpropion has minimal potential for abuse.

Tenuate—it makes sense. And it's responsible medicine.

Merrell

For prescribing information see opposite page

new
600 mg tablets
Motrin®
ibuprofen, Upjohn

More convenient for
some of your patients.

Now there are three
Motrin tablet strengths
to choose from-
600 mg, 400 mg, and 300 mg

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001, U.S.A.

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In Edema* or Hypertension* when potassium balance is a concern...

Potassium-Sparing

DYAZIDE®

Each capsule contains 50 mg. of Dyrenium® (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Makes Sense

In Edema

The triamterene in 'Dyazide' limits potassium loss and provides an additive diuretic effect to that of the hydrochlorothiazide component.

In Hypertension

As the hydrochlorothiazide in 'Dyazide' lowers blood pressure, the triamterene component limits potassium loss.

Serum K⁺ and BUN should be checked periodically particularly in the elderly, diabetics, and those with suspected or confirmed renal insufficiency (see Warnings). If hyperkalemia develops, substitute a thiazide alone.

Before prescribing, see complete prescribing information in SK&F Co. literature or *PDR*. A brief summary follows:

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K⁺ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K⁺ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K⁺ frequently; both can cause K⁺ retention and elevated serum K⁺. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

SK&F CO.
a SmithKline company

SK&F CO.
Carolina P.R. 00630

EMPIRIN® COMPOUND
c̄ CODEINE

Each tablet contains: aspirin, 227 mg; phenacetin, 162 mg; and caffeine, 32 mg; plus codeine phosphate in one of the following strengths: #4—60 mg (gr 1); #3—30 mg (gr ½); #2—15 mg (gr ¼); and #1—7.5 mg (gr ⅛), (Warning—may be habit-forming). CIII

Wellcome
Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

IT WAS MOVED AND CARRIED TO ACTIVELY STUDY S.B. 1248

H.B. 2219 - Hospital Licensing

H.B. 2219 would allow the Department of Health Services to accept proof that a health care institution is an accredited hospital in lieu of requiring inspection for licensure. An accredited hospital would be defined under this bill as a hospital currently accredited by the joint commission on accreditation of hospitals or the commission on accreditation of the American Osteopathic Association. It was noted that this bill has passed in the House.

IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO H.B. 2219.

H.B. 2220 - Hospital Expansion

H.B. 2220 prescribes the definition of "capital expenditure" and established a new set of conditions for the issuance of a health care institution certificate of need. Mr. Chic Older of the Arizona Hospital Association informed the committee that this is a redo of an ArHA bill introduced last year and that it will significantly streamline the certificate of need laws.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT H.B. 2220

H.B. 2334 - Hospital Regulation

H.B. 2334 provides that in the establishing of rules and regulations for licensure of health care institutions, the Director of the Department of Helath Services consider the estimated costs and corresponding benefits of such regulations to health care institutions and to patients of health care institutions and, further, issue findings regarding such costs and benefits prior to the adoption, repeal or amendment of such rules and regulations.

IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO H.B. 2334.

H.B. 2374 - Hospital Statute Corrections

Mr. Older of the Arizona Hospital Association informed the committee that the purpose of H. B. 2374 is to correct a defective 1973 legislative enactment relating to health care institutions.

IT WAS MOVED AND CARRIED TO RECEIVE H.B. 2374 FOR INFORMATION ONLY.

H.B. 2337 - Hospital Regulation Penalty

H.B. 2337 provides that any licensed health care institution which violates certain laws so as to cause injury or material neglect of any patient or fail to maintain reasonable care to treatment of any patient may be assessed a civil penalty by the Director of the Department of Health Services.

IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO H.B. 2337.

H.B. 2198 - Health Records

H.B. 2198 would provide that a patient is the owner of his own health records and that the health care provider, in effect, would be the custodian rather than the owner of such records.

IT WAS MOVED AND CARRIED TO GIVE VIGOROUS ACTIVE NON-SUPPORT TO H.B. 2198.

S.B. 1292 - Children Health Services

S.B. 1292 would replace the existing enabling statutory authority for the Arizona medicaid program with a program of comprehensive health care services for children. Under this bill, children would be defined as persons 21 years of age and under.

IT WAS MOVED AND CARRIED TO ACTIVELY STUDY S.B. 1292

S.B. 1332, H.B. 2360 - Indigents Health Care

S.B. 1322 and H.B. 2360, if passed, would repeal the present medicaid law and provide for a joint legislative study committee on health care services for the medically needy.

IT WAS MOVED AND CARRIED TO GENERALLY SUPPORT S.B. 1322 AND H.B. 2360.

H.C.R. 2011 - Right to Life

H.C.R. 2011 would urge Congress to call a constitutional convention to propose an amendment to the constitution of the United States to protect the right to life of all human beings. This resolution provides that a human being shall be deemed from the moment of fertilization to be a person and entitled to the right to life.

IT WAS MOVED AND CARRIED TO GIVE GENERAL NON SUPPORT TO H.C.R. 2011.

H.B. 2292 - Public Funded Abortions

H.B. 2292 would provide that no public funds would be expended for the performance of any abortion unless an abortion is necessary to save the life or prevent the serious impairment of the health of the woman having the abortion or if the pregnancy was the result of sexual assault or sexual intercourse between persons whose marriage would be prohibited and void under the present law.

IT WAS MOVED AND CARRIED TO GIVE GENERAL NON-SUPPORT TO H.B. 2292.

H.B. 2157 - Uniform Controlled Substance Act

H.B. 2157 would enact the uniform controlled substances act (UCSA) in the State of Arizona. Under this bill, existing state laws relating to narcotics and dangerous drugs would be repealed. However, existing law relating to marijuana would be left unchanged. In the place of those state laws relating to narcotic and dangerous drugs, which conflict in several respects with the provisions of federal law, this bill would establish a coordinated system of drug control, following federal law which would classify all narcotics and dangerous drugs and controlled substances subject to control into five schedules with each schedule having certain specific criteria for drug placement.

IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO H.B. 2157.

H.B. 2288 - Generic Drugs

H.B. 2288 would allow a pharmacist, when permitted to substitute, with another drug having the same active chemical ingredients of the same strength, quantity and dosage and of the same generic drug type as the brand name drug perscribed as opposed to the present law which permits substitution with a generic drug biologically, chemically, and therapeutically equivalent to the brand name drug. It would repeal the present requirement for the formulary of generic drugs. The Chairperson pointed out that this bill does not mandate that in cases of generic substitution, proportional savings be passed on to the consumer. There was discussion.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT H.B. 2288.

IT WAS MOVED AND CARRIED TO SUPPORT THE INCLUSION IN THE CURRENT LAW THAT PROPORTIONAL SAVINGS BE PASSED ON TC THE CURRENT LAW THAT PROPORTIONAL SAVINGS BE PASSED ON TC THE CONSUMERS IN CASE OF GENERIC DRUG SUBSTITUTION.

H.B. 2200 - Autopsy Corneal Transplant

H.B. 2200 would permit a county medical examiner to authorize the taking of corneal tissue from a decedent upon the request of an authorized official of an eye bank or storage facility or the licensed physician of a patient in need of corneal tissue for a transplant provided the decedent died under circumstances requiring an inquest by the county medical examiner and no objection by the decedent's next of kin is known. It was noted that cases requiring an inquest are not numerous, therefore the supply of corneal tissue would be limited. Amending the bill to read cases requiring an examination by the county medical examiner, rather than inquest, would increase the amount of corneal tissue available.

IT WAS MOVED AND CARRIED TO GENERALLY SUPPORT H.B. 2200 IF AMENDED TO AUTHORIZED THE TAKING OF CORNEAL TISSUE IN CASES REQUIRING AN EXAMINATION BY THE COUNTY MEDICAL EXAMINER.

H.B. 2201 - Paternity Blood Test

H.B. 2201 provides for blood tests in maternity and paternity proceedings and for the payment for costs of the blood tests.

IT WAS MOVED AND CARRIED TO RECEIVE H.B. 2201 FOR INFORMATION ONLY.

H.B. 2402 - Doctors Insurance Association

H.B. 2402 provides that physicians' insurance administration association such as the Maricopa and Pima Foundations would be exempt from the state anit-trust laws provided the purpose of the corporaton is to reduce the cost of medical services provided under group heatlh insurance to a level below that of the usual and customary charges by physicians. This bill was passed in the House Banking and Insurance Committee but held on a 7-7 vote in the Professions, Occupations and Tourism Committee. House Marjority Leader Burton Barr, the sponsor of the bill, will have this bill reconsidered at a later date. This bill has been received and reviewed by the Board of Directors; they have determined that the Arizona Medical Association will actively support H.B. 2402.

IT WAS MOVED AND CARRIED TO RECEIVE H.B. 2402 AND THE BOARD OF DIRECTOR'S ACTION TO ACTIVELY SUPPORT H.B. 2402 FOR INFORMATION ONLY.

H.B. 2222 - Health Services Insolvencies

H.B. 2222 would expand the coverage of the life and disability insurance guaranty fund to include health care services (HMO's). Although HCSO's are not, by definition, insurers under present state law, all HCSO's authorized to do business in this state would be required to be members of the reconstituted life, disability insurance and health care services organizaiton guaranty fund under this bill. Impaired HCS's would thus be subject to the same security guarantees as are life and disability insurers under existing state law. It was noted that this bill was passed in the House Health Committee.

IT WAS MOVED AND CARRIED TO GENERALLY SUPPORT H.B. 2222.

H.B. 2339 - Alcoholism, Mental Illness and Drug Abuse Insurance

H.B. 2339 would require most types of health services coverages and health insurance policies offered in this state to contain coverage, after January 1, 1980, for the treatment of alcoholism, mental illness and drug addiction. There is no requirement that coverage for these illnesses be included as part of the required coverage of any health service contract or insurance policy under existing law. It was noted that the Arizona Medical Association has supported this type of legislation in the past.

IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO H.B. 2339.

H.B. 2436 - Psychologist Insurance

H.B. 2436 would provide that benefits for services performed by certified or licensed psychologist to be excluded from subscription contracts of hospital and medical service corporations, disability insurance contracts or group and blanket disability insurance contracts.

IT WAS MOVED AND CARRIED TO GENERALLY NON-SUPPORT H.B. 2436.

H.B. 2333 - Behavioral Health Treatment

H.B. 2333 would expand behavioral health treatment services in the State of Arizona. There was considerable discussion with regard to specific rules and regulations this bill would establish if passed into law. It was determined that this bill contains both supportable and opposable elememts.

IT WAS MOVED AND CARRIED TO ACTIVELY STUDY H.B. 2333.

IT WAS MOVED AND CARRIED TO SUPPORT THE CONCEPT OF INCREASED STATE SERVICES IN THE BEHAVIORAL HEALTH SERVICES AREA.

S.B. 1210 - Study Council on Health Care Laws

S.B. 1210 would establish a study council on health care laws and regulations for the purpose of investigating and recommending changes in the health care laws and regulations as they affect families, children and youth. The study council would be required to file a comprehensive final report on or before January 1, 1980.

IT WAS MOVED AND CARRIED TO TAKE NO ACTION ON S.B. 1210

S.B. 1250 - Homeopathic Physicians

S.B. 1250 would allow homeopathic physicians the right to practice in the State of Arizona. This legislation would establish a board of homeopathic medical examiners and provide for licensing and regulation of homeopathic physicians.

IT WAS MOVED AND CARRIED TO ACTIVELY NON-SUPPORT S.B. 1250.

H.B. 2420 - Kidney Center Tax Exemption

H.B. 2420 would provide a sales tax exemption for personal property purchased or leased by a kidney dialysis center.

IT WAS MOVED AND CARRIED TO GIVE GENERAL SUPPORT TO H.B. 2420.

H.B. 2407 - Optometry; Use of Pharmaceutical Agents

Dr. Thomas Moore informed the committee of the introduction of H.B. 2407 which, if passed, would allow optometrists to use diagnostic pharmaceutical agents for diagnosis purposes after first completing a course in pharmacology.

IT WAS MOVED AND CARRIED TO GIVE VIGOROUS ACTIVE NON-SUPPORT TO H.B. 2407.

H.B. 2036 - Pesticides

Dr. Suzanne Dandoy explained to the committee that H.B. 2036 would prescribe that the State Chemist and Director of the Department of Health Services become members of the board of pesticide control. This would provide medical input into the regulation of pesticides in the state. The bill would also give the Director of the Department of Health Services broader control over the use of pesticides, thus being better able to protect the health of the people of the state.

IT WAS MOVED AND CARRIED TO ACTIVELY SUPPORT THE CONCEPT OF MEDICAL INPUT INTO PESTICIDE CONTROL ACTIVITIES.

EXECUTIVE COMMITTEE

The meeting of the Executive Committee of the Arizona Medical Association, Inc. held at 810 West Bethany Home Road, Phoenix, Arizona, on Friday, March 23, 1979, a quorum being present, convened at 6:40 p.m., Richard L. Dexter, M.D., President and Chairman, presiding.

U.S. SENATE CANDIDACY

Frank J. DePaoli, Jr., M.D. advised the committee that he will, most likely, in the near future be announcing his candidacy for the U. S. Senate. Dr. DePaoli discussed what he felt was a very defined need to have a physician in office in order to have qualified and well-versed representation for the medical profession as a hole.

ArMPAC CHAIRMANSHIP

Following a lengthy discussion regarding the need to immediately find a qualified, hard-working individual who would and could accept the chairmanship of ArMPAC, it was agreed that Dr. Crisp would meet and talk with Richard O. Flynn, M.D., to determine his feelings regarding such appointment.

Additionally, it was agreed that the ArMA Auxiliary would be contacted to see if anyone among their membership had expressed any desire to possibly accept such a position.

LEGISLATIVE UPDATE

Gary Barnett presented to the committee an update of all legislation which had been presented to or was being considered by the Legislature in which ArMA and its membership had an interest, reporting in depth on the bills pending regarding the JUP, optometric drugs and podiatry.

WPPA PROGRAM - LEASING VS. PURCHASING

Dr. Kahle reported on a recent meeting in Cheyenne regarding a possible program for inclusion during ArMA's Annual Meeting in April. The program would be presented by a representative from Scherer Corporation for and on behalf of the WPPA regarding leasing vs. purchasing.

Following a discussion, it was felt that the presentation should be made if at all possible and Mr. Robinson was requested to made whatever arrangements he could with the Safari Hotel and Scherer, through WPPA office in Cheyenne.

AMERICAN ASSOCIATION OF MEDICAL SOCIETY EXECUTIVES

The committee reviewed a memorandum from AAMSE dated March 5, 1979 containing names of nominees for election to the American Association of Medical Society Executives Board of Directors, one of which was Bruce E. Robinson.

IT WAS MOVED AND CARRIED THAT THE EXECUTIVE COMMITTEE APPROVE THE NOMINATION OF BRUCE E. ROBINSON TO THE BOARD OF DIRECTORS OF THE AMERICAN ASSOCIATION OF MEDICAL SOCIETY EXECUTIVES, WHICH NOMINATION IS FOR A TWO-YEAR TERM AND UNDERWRITE THE EXPENSES RELATED THERETO.

Nominees for the Board of Directors

Mr. Robinson advised the committee that it had come to his attention certain nominees to fill vacancies on the Board of Directors had failed to pay their 1979 dues. It was the consensus of opinion that those physicians should be contacted and reminded that their dues must be current prior to their election to or service on the Board.

CORRESPONDENCE

Appreciation Letter

The letter of Thomas E. Moon, Ph.D., dated March 16, 1979, regarding the Cancer Center Newsletter - RECEIVED.

OTHER BUSINESS

Status of Lawsuit

Bruce E. Robinson briefly reported on the current status of ArMA's lawsuit filed against the State Attorney General, advising the committee that discovery was underway on behalf of both parties, which presently consisted of answering and submitting interrogatories, requests for admissions and requests to produce documents.

Unified Membership

Dr. Clymer presented to the committee a form letter for possible distribution to physicians regarding unified membership, which would again be considered by the House of Delegates at ArMA's annual meeting in April. Following a lengthy discussion,

IT WAS MOVED AND CARRIED THAT A LETTER BE SENT TO ALL PHYSICIANS IN THE STATE ADVISING THAT THE QUESTION OF UNIFIED MEMBERSHIP WOULD BE HEARD BY THE HOUSE OF DELEGATES DURING THE ANNUAL MEETING OF THE ARIZONA MEDICAL ASSOCIATION, THAT THE REFERENCE COMMITTEE RELATIVE TO THAT QUESTION WOULD MEET AT 2:00 P.M. ON WEDNESDAY, APRIL 25, 1979, AT THE SAFARI RESORT IN SCOTTSDALE, ARIZONA, AND THAT ANY AND ALL PHYSICIANS WERE WELCOME TO APPEAR AND GIVE TESTIMONY FOR OR AGAINST UNIFIED MEMBERSHIP.

"Official Family" Briefing

Discussion was held regarding the finalization of plans for the holding of the "Official Family" Briefing Session to be held at the Safari Resort at 7:30 p.m., Tuesday, April 24, 1979, and it was the consensus of opinion that additional letters of invitation be extended to all members of the House of Delegates.

AMA WORKSHOP

The committee reviewed an invitation received by Dr. Clymer to participate in a "Physicians and Chronic Mental Patients: Potentials for Community Based Care" workshop scheduled for May 10-11, 1979 in Chicago.

IT WAS MOVED AND CARRIED APPROVING THE ATTENDANCE BY JOHN T. CLYMER, M.D. AT THE WORKSHOP ENTITLED "PHYSICIANS AND CHRONIC MENTAL PATIENTS: POTENTIALS FOR COMMUNITY BASED CARE" SCHEDULED TO BE HELD IN CHICAGO, MAY 10-11, 1979.

Future Medical Meetings

CONTINUING MEDICAL EDUCATION

The following institutions and organizations have been accredited for their continuing medical education programs by the Liaison Committee on Continuing Medical Education.

Arizona Heart Institute
Arizona Medical Association, Inc.
Arizona State Hospital, Phoenix
Desert Samaritan Hospital, Mesa
Good Samaritan Hospital, Phoenix
Health Maintenance Associates, Phoenix
Maricopa County General Hospital, Phoenix
Mesa Lutheran Hospital, Mesa
Phoenix Baptist Hospital & Health Center
Phoenix Indian Medical Center
Phoenix Memorial Hospital
Phoenix Psychiatric Council
St. Joseph's Hospital & Medical Center, Phoenix
Barrow Neurological Institute, Phoenix
St. Lukes's Hospital & Medical Center, Phoenix
Scottsdale Memorial Hospital
Tucson Medical Center & Kino Community Hospital, Tucson
Veterans Administration Hospital, Phoenix
Veterans Administration Hospital, Prescott
University of Arizona College of Medicine, Tucson

The accredited institutions and organizations above produce a variety of continuing medical education programs. Each accredited institution and organization is responsible for designating which of these programs meet ArMA's requirements for Category 1 credit. Physicians who participate in programs which are designated Category 1 by accredited institutions will receive Category 1 credit toward the ArMA Certificate in CME and the AMA's Physician's Recognition Award.

MAY

First Annual Symposium on Current Concepts in the Management of Acute and Chronic Pain
May 19, 1979. Registry Resort, Scottsdale Arizona.Sponsor: Maricopa County General Hospital, Phoenix, AZ; Dept. of Anesthesiology & Dept. of Continuing Medical Education. Contact: Anesthesiology Dept., Maricopa County General Hospital, 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 10 hours of category 1 credit.

Medical History Society of Arizona.
Tuesday, May 29, 1979, 7:30 p.m., Preston T. Brown Room of Maricopa County Medical Society, 2025 N. Central Ave., Phoenix, AZ. Contact: William C. Weese, M.D., President 265-0000.

JUNE

Current Concepts in Obstetrics & Gynecology and their Clinical Applications
June 14-16, 1979. Santa Fe Hilton Inn, Santa Fe, N. M. 87501. Sponsor: Symposia de Santa Fe & New Mexico Medical Society. Contact: Walter J. Levy, M.D. P.O. Box 5175, Santa Fe, N.M. 87502. Approved for 16 ½ hours of prescribed CME credit.

Advanced Cardiac Life Support - Provider
June 22 & 23, 1979. Arizona Medical Association offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner, ArMA Offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Approved for 16 hours of category 1 credit.

JULY

22nd Annual Ruidoso Family Practice Seminar
July 16-19, 1979. Inn of the Mountain Gods, Mescalero, New Mexico. Sponsor: New Mexico Chapter of the American Academy of Family Physicians. Contact: Bob Reid, Chairman, P.O. Box 456, Sunland Park, N.M. 88063. Approved for CME credit hours.

Advanced Cardiac Life Support Program - Provider
July 20 & 21, 1979. Arizona Medical Association offices, 810 W. Bethany Home Rd., Phoeix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner, ArMA Offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Approved for 16 hours of category 1 credit.

MONTHLY OR WEEKLY

Shrine Medics Meeting
Second Tuesday of each month, Doctors Hospital; 5:45 p.m. J. South Classroom. Sponsor: Shrine Medics. Contact: Robert C. Briggs, M.D., 5121 N. Central Ave., Phoenix, AZ 85012.

Office Psychiatry for the Primary Provider
2nd Monday of month, 4811 N. 7th Street, Phoenix, AZ. Sponsor: Arizona Health Plan. Contact: T.R. Bittker, M.D., Box 5000, Phoenix, AZ 85010. Approved for category 1 credit.

Counter Transference Group
Weekly, Thurs. 8—10 p.m. Sponsor: Phoenix Psychiatric Council. Contact: James E. Campbell, M.D., 5051 N. 34th St., Phoenix, AZ 85018. Approved for 2 hours category 1 credit.

Monthly Meeting of Tucson Radiologists
Last Tues. of month. Plaza International, Tucson, AZ. Sponsor: U of A Medical Center, Dept. of Radiology. Contact: Irwin M. Freundlich, M.D., U of A Health Sciences Center, Dept. of, Radiology, Tucson, AZ 85724. Approved for 2 hours category 1 credit.

Pediatric Grand Rounds
Tuesday 7:30-8:30 a.m in Phoenix: 1st Tues.—Phoenix Indian Hospital, 2nd Tues.—Maricopa County Hospital, 3rd Tues.—Good Samaritan Hospital, 4th Tues.—St. Joseph's Hospital. Sponsor: Maricopa County Hospital (Phoenix Hospital's Affiliated Pediatric Program). Contact: J. Kipp Charlton, M.D., 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

Review of Forensic Pathology Current Case, Special Topics
Thursday, weekly, 11 a.m., 120 S. 6th Ave., Phoenix, AZ. Sponsor: Arizona Society of Pathologists. Contact: H.H. Karnitschnig, M.D., 120 S. 6th Ave., Phoenix, AZ. Approved for 1 hour per session category 1 credit.

Staff Education Conference
Wednesdays, weekly, 1 p.m., Arizona State Hospital, Phoenix, AZ. Sponsor: Arizona State Hospital. Contact: Howard E. Wulsin, M.D., Arizona State Hospital, 2500 E. Van Buren, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

BARROW NEUROLOGICAL INSTITUTE

Medical Education
Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Sponsor: St Joseph's Hospital & Medical Center. Contact: John R. Green, M.D. Approved for 1 hour category 1 credit.

Neurology Teaching Conference
Tuesdays, 8:30-9:30 a.m., Eighth Floor Conf. Room.

Neurosurgery Morbidity Conference
Wednesdays, 8:15-9:15 a.m., on first and third weeks, Eighth Floor Conference Room.

Neuro-ophthalmology Conference
Tuesdays, 7:30 a.m. in 8th floor neurology conference room.

Spinal Injury Conference
Wednesdays, 8:15-9:15 a.m., on second and fourth weeks, in Neuropathology Conf. Rm.—a multidisciplinary review of admission by neurosurgeons, orthopedists, and rehabilitation specialists

Neuropathology of Gross Specimens Conference
Thursday, 7:30-8:30 a.m. in the Morgue.

Neurology-Neurosurgical Clinical-Neuroradiological and Neuropathological Conference
Fridays,'8-9 a.m., First Floor Conference Rm.

Neuropathology or Neuroradiology Conferences
Friday, 9 a.m., Neuropathology in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

Neurorehabilitation Conference
Tuesdays, noon, 8th Floor Conference Rm.

Neurosurgical Journal Club
Saturdays, 9-11 a.m. in Eighth Floor Conference Rm.

CAMELBACK HOSPITAL

5055 N. 34th St., Phoenix, AZ 85018. Sponsor: Camelback Hospital. Contact: Medical Director.

Patient Staffing Conference
Three times weekly.

DESERT SAMARITAN HOSPITAL

Wednesday evenings, 7 p.m. Sponsor: Desert Samaritan Hospital. Contact: L. A. Rosati M.D., Laboratory, Desert Samaritan Hospital, Mesa, AZ 85202. Approved for category 1 credit.

GOOD SAMARITAN HOSPITAL

Clinical Cancer Conference
3rd Wednesday, every month, Butler Bldg. Conference Rm. Good Samaritan Hospital. Contact: John A. Bruner, M.D., 926 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour per session category 1 credit.

Pulmonary Disease Grand Rounds
Mondays, 12 Noon, D-5 North Conf. Rm., Good Samaritan Hospital, Phoenix, AZ. Sponsor: Pulmonary Disease Teaching Service, Good Samaritan Hospital. Contact: Bernard E. Levine, M.D., Pulmonary Function Laboratory, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour category 1 credit.

MARYVALE SAMARITAN HOSPITAL

Continuing Medical Education Program
Maryvale Samaritan Hospital, every other Wednesday, 7-8 a.m.

MARICOPA COUNTY GENERAL HOSPITAL

2601 E. Roosevelt, Phoenix, AZ 85008. Sponsor: Maricopa County General Hospital. Contact: H. F. Lenhardt, M.D., Dir. of Medical Education. Approved for category 1 credit.

The Hand Surgery Conference
Wednesday 7:30 a.m., Santa Cruz Room, Maricopa County Hospital.

MEMORIAL HOSPITAL

1201 S. 7th Ave., Phoenix, AZ 85036. Sponsor: Memorial Hospital. Approved for category 1 credit.

Month Medical Education Seminar
Third Monday, 6:30 p.m., Kiva Conference Rm. Contact: George Scharf, M.D.

Tumor Board Conference
Every Friday at Noon, Kiva Conference Rm. Contact: Howard Kimball, M.D.

SCOTTSDALE MEMORIAL HOSPITAL

7300 E. 4th St., Scottsdale, AZ 85251. Sponsor: Scottsdale Memorial Hospital. Contact: W. S. Wiliams, M.D., Director of Medical Education

Clinical Pathological Conference
4th Monday, monthly, 12:45 p.m.

Family Practice Conference
1st Monday, monthly, 12:45 p.m.

Medical Grand Rounds
3rd Monday, monthly, 12:45 p.m.

Morbidity & Mortality Conference
2nd Monday, monthly, 12:45 p.m.

ST MARY'S HOSPITAL & HEALTH CENTER

1601 W. St. Mary's Rd., Tucson, AZ 85703. Sponsor: St. Mary's Hospital & Health Center. Contact: see below.

Cardiology Conference
Every Friday 8-9 a.m., Century Rm. A. Contact: Anthony L. Forte, M.D.

Monthly Specialty Conference of the Department of Surgery
First Monday, monthly, 7:30 a.m. Century Rm. A. Contact: Medical Staff Office. Approved for 1 hour of category 1 credit

Grand Rounds: Medical Surgical, Family Practice, Pathology, Radiology
Weekly, Thursday, 7-8:30 a.m. Contact: Richard A. Silver, M.D. Approved for 1 hours of category 1 credit.

U OF A HEALTH SCIENCES CENTER

Sponsor: U of A College of Medicine, Tucson, AZ 85724. Contact: See below. Approved for category 1 credit.

Clinical Immunology, Allergy & Rheumatology Rounds
Every Friday, Noon-1 p.m. Contact: John Boyer, M.D., Dept. of Internal Medicine.

Cerebrovascular Disease Conference
Mondays, 5-6 p.m., weekly, Rm. 5505. Contact: Wesly Moore, M.D.,Depts. of Surgery, Nurology & Radiology.

Dean's Clinical Rounds
Contact: Louis J. Kettel, M.D.

Endocrinology Seminar
Every Thursday, Noon-1 p.m., 1st, 3rd & 5th Thursday, Room N318, VA Hospital. 2nd & 4th Thursday, Room 6505, Tucson Medical Center. Contact: Dept. of Internal Medicine.

Hematology-Oncology Clinical Conference
Every Tuesday, Noon-1 p.m., 1st, 3rd & 5th Tuesdays, Rm 6505, Tucson Medical Center. 2nd & 4th Tuesdays, Rm. N318, VA Hospital. Contact: Sidney Salmon, M.D., Dept. of Internal Medicine.

Joint Thyroid Clinic Conference
1st & 3rd Mondays of every month.1 to 2 p.m., AHSC,Rm. 6505. Contact: Sidney Werner, M.D., Dept. of Internal Medicine, Endocrinology Section.

Medical Grand Rounds
Every Wed., Noon-1p.m., 1st, 3rd, & 5th Wed., Staff Conf. Room, VA Hospital. 2nd & 4th Wed.,Rm. 5403, UAHSC. Contact: Jay Smith, M.D., Dept. of Internal Medicine.

Nuclear Medicine
Thursday, 7:30 a.m., Radiology Conf. Rm., UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Diagnostic Radiology.

Neurology Grand Rounds
Every Friday, Noon, 1st, 3rd, & 5th Fridays, UAHSC, Rm. 7505. 2nd & 4th Fridays, VA Hospital. Contact: William A. Sibley, M.D., Dept. of Neurology.

Neuropathology Review Conference
Thursdays, 8:30 a.m., Rm. 5120, UAHSC. Contact: Peter C. Johnson, M.D.

Neurosciences Seminar
Every Friday, 7:30 a.m.,UAHSC, Rm 7505. Contact: Colin R. Bamford, M.D., or Jose F. Laguna, M.D., Dept. of Neurology.

Pathology Seminar
Friday, 4:30-5:30 p.m., Rm. 5120, UAHSC. Contact: Paul Finley, M.D., Dept. of Pathology.

Tucson Pathologist Conference
First Monday of the Month, 7:30-9 p.m. Rotation between Tucson Pathology Conf. Rms. Contact: Anna Graham, M.D., Tucson Pathologists.

Pediatric Grand Rounds
Every Tuesday, 12:30-1:30 p.m. Alternates between Tucson Medical Center & UAHSC. Contact: Hugh Thompson, M.D., Dept. of Pediatrics.

Problem Case Workshop
3rd Monday of each month, 7:30 a.m., Rm 4410, UAHSC. Contact: H. E. Cross, M.D., Ph.D., Div. Of Ophthalmology.

Psychiatric Grand Rounds
Every Wednesday, Sept. to May 4, 5:30 p.m., Rm8403 UAHSC. Contact: Alan Levenson, M.D., Dept. of Psychiatry.

Chest Radiology
Monday, 5-6 p.m., weekly, Rm 1535F, UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Gastrointestinal Radiology
Mondays, 7:30 a.m., weekly except for summer months. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Radiation Oncology Planning Conference
Friday, weekly, 8:30-10 a.m., UAHSC, Rm. 0655. Contact: Robert S. Heusinkveld, M.D., Radiation Oncology Section.

Radiology-Rheumatology Conference
Thursday, 8 a.m., UAHSC, Library Rm.1535C. Contact: Irwin M. Freundlich, M.D. Dept. of Radiology.

Vascular Radiology
Radiology Interesting Case Conference
Thursday, Noon, VA Hospital. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Resident's Conference
Wednesday, weekly 5-6 p.m., Diag. Radiology Conf. Rm. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology

Trauma Conference
Every Thursday,4-5 p.m. UAHSC, Rm. 5505. Contact: Martin Silverstein, M.D., Dept. of Surgery.

Grand Ward Rounds—Trauma
Every Tuesday, 8 a.m., UAHSC. Contact: Martin Silverstein, Surgery Dept., Trauma Section.

Monthly Meeting Tucson Ultrasonography Group
First Wed. of month, 4:30-5:30 p.m., UAHSC. Contact: Irwin M. Freundlich, M.D.

Tucson Urological Society Scientific Meeting
Monthly. Contact: George W. Drach, M.D., Depts. of Surgery & Urology.

General Urology Conference
Tuesday 5-6 p.m. Thursday, Noon-1:30 p.m. UAHSC Meeting Rooms & VA Hospital. Contact: George W. Drach, M.D., Dept of Surgery/Urology Section.

VETERANS ADMINISTRATION HOSPITAL

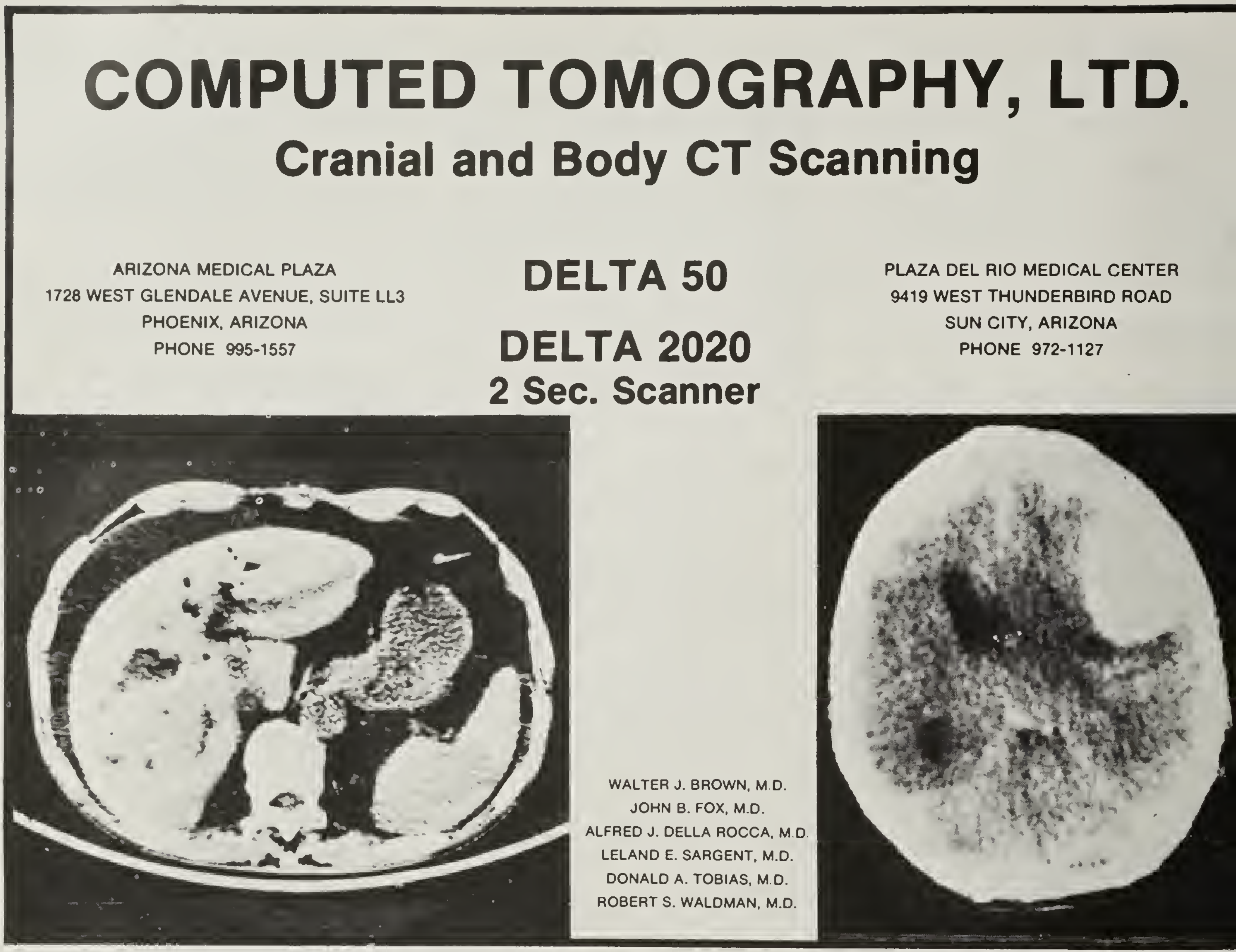
7th St. and Indian School Rd., Phoenix, AZ 85012. Sponsor: VA Hospital. Contact: Jasper L. McPhail, M.D. Approved for Category 1 credit.

Academic Surgery Conference
Each Thursday — 2 p.m. — C435, Dr. Cannon, Ext. 493.

Cardiology Conference
2nd Thursday — 1 p.m. — T5, Dr. Habibzadeh, Ext. 348.

Cancer Symposium
Each Wednesday — 1 p.m. — T5, Dr. Berkley, Ext. 419.

Clinical Conference
4th Thursday of 3rd Month, (Mar. Jun., Sept., & Dec.), 1 p.m. — T5, Dr. Likos, Ext. 623.



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Dermatology Conference
1st, 2nd, & 3rd Wednesday (usually, but is subject to change) 10 a.m. — C118, Dr. Roberts, Ext. 426.

G.I. Radiology Clinical Correlation Conference 1st & 3rd Monday — 1 p.m. — C435, Dr. Sanowski, Ext. 618.

G.I. Grand Rounds
Ech Tuesday — 1 p.m. — T5, (4th Thursday with U of A Consultants) Dr. Sanowski, Ext. 618.

Medical Service Grand Rounds
Each Friday — 11 a.m. — T5, Dr. Zeller, Ext 272

Medical-Surgical Chest Conference
1st and 3rd Thursday — 1 p.m. — T5, Dr. Chowdhury, Ext. 388.

Medical-Surgical G.I. Conference
Ist & 3rd Friday — 2 p.m. — 2123, Dr. Sanowski, Ext. 618.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery-Pathology Conference
Each Thursday — 2 p.m. — 2128, Dr. Cannon, Ext 493, & Dr. Likos, Ext. 623.

Urology-Pathology Conference
Each Wednesday — 7 a.m. — 2128, Dr. Likos, Ext. 623 & Dr. Pentenney, Ext., 417.

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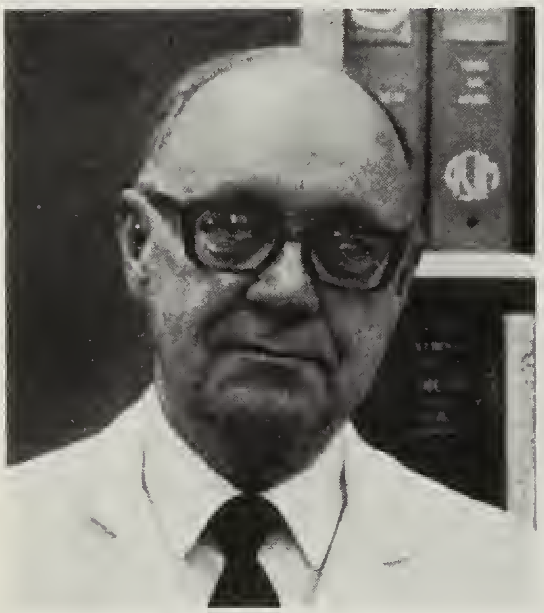
—Dr. William Felts, Past President,
American Society of Internal Medicine



More and more physicians today are beginning to realize the extent of the economic influence they have, and are finding ways of holding costs down.

A number of studies show that the more physicians *know* about costs, the more they try to *reduce* them.* And this reduction can be done without reducing the quality of care to the patient.

How are they doing this? As a start they have become thoroughly familiar with the costs they incur on behalf of their patients. They know how much an X-ray costs, how much their hospital charges for routine lab tests. They're requesting copies of patients' hospital bills. And asking their hospitals to print the charges for diagnostic tests right on the order sheet.

What else are physicians doing? Minimizing their patients' hospital stays, whenever possible. Reevaluating routine admissions procedures. Questioning the real need of the diagnostic tests they order for their patients. Avoiding duplicate testing. Trying to discourage their patients' demands for unnecessary medication, treatment or hospitalization. Compiling daily logs of their medical decisions and what they cost. And more.

More physicians today realize what a tough problem we're all faced with. They know this is a challenge for medicine. And that physicians are in the best position to deal with and solve the problem.

**PATIENT CARE Magazine—Outlook 1977, "Face-Off: Cost Containment vs. Chaos," January 1, 1977.*

Lyle CB, et al. "Practice habits in a group of eight internists," ANNALS OF INTERNAL MEDICINE 84 (May 1976), 594-601.

Schroeder SA, et al. "Use of laboratory tests and pharmaceuticals: variation among physicians and effect of cost audit on subsequent use," JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 225 (Aug. 20, 1973), 969-73.

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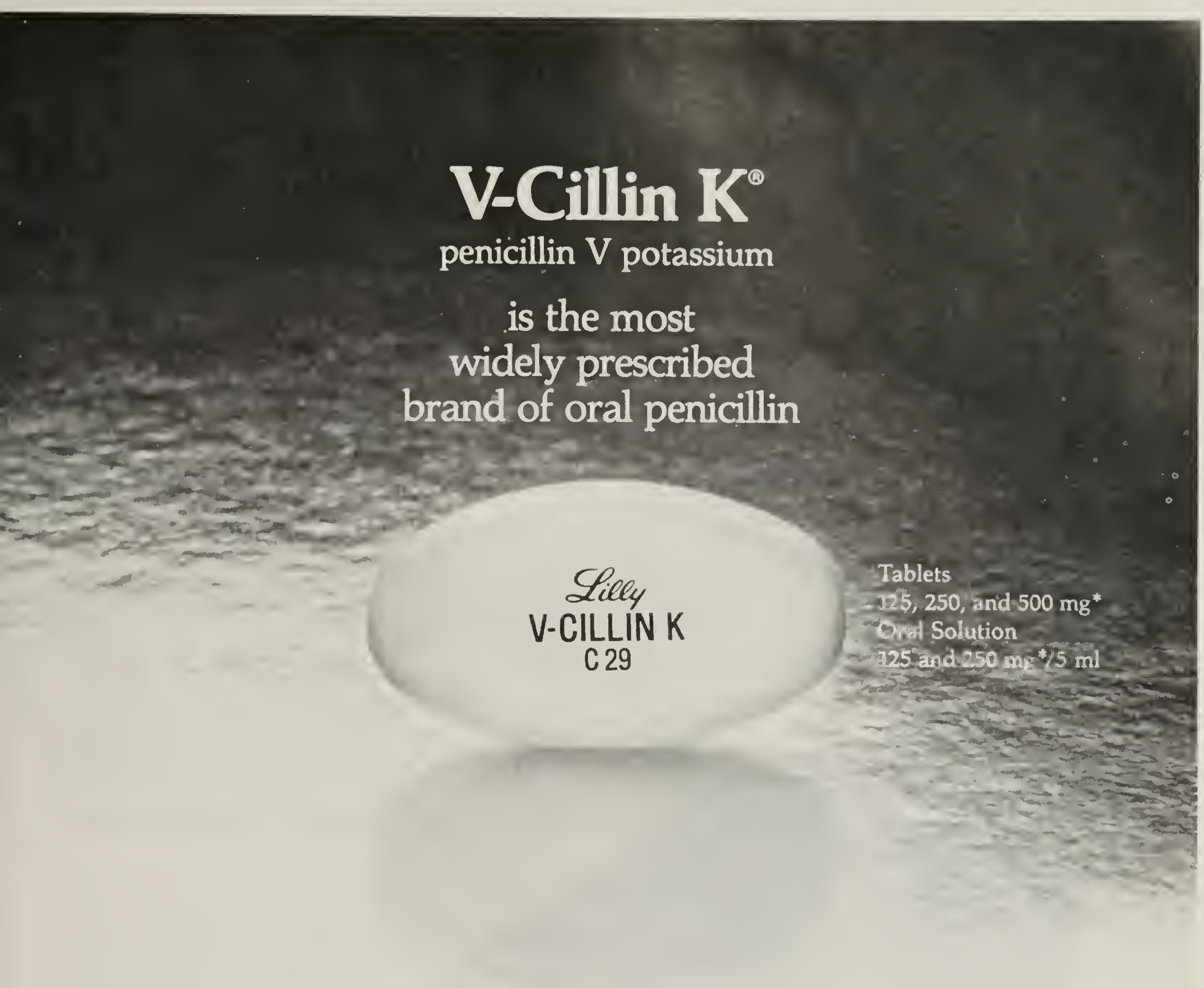

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Precautions: Use with caution in individuals with histories of significant allergies and/or asthma. Do not rely on oral administration in patients with severe illness, nausea, vomiting, gastric dilatation, cardiospasm, or intestinal hypermotility. Occasional patients will not absorb therapeutic amounts given orally. In streptococcal infections, treat until the organism is eliminated (minimum of ten days). With prolonged use, nonsusceptible organisms, including fungi, may overgrow; treat superinfection appropriately.

Adverse Reactions: Hypersensitivity, including fatal anaphylaxis. Nausea, vomiting, epigastric distress, diarrhea, and black, hairy tongue. Skin eruptions, urticaria, reactions resembling serum sickness (including chills, edema, arthralgia, prostration), laryngeal edema, fever, and eosinophilia. Infrequent hemolytic anemia, leukopenia, thrombocytopenia, neuropathy, and nephropathy, usually with high doses of parenteral penicillin. [102175]

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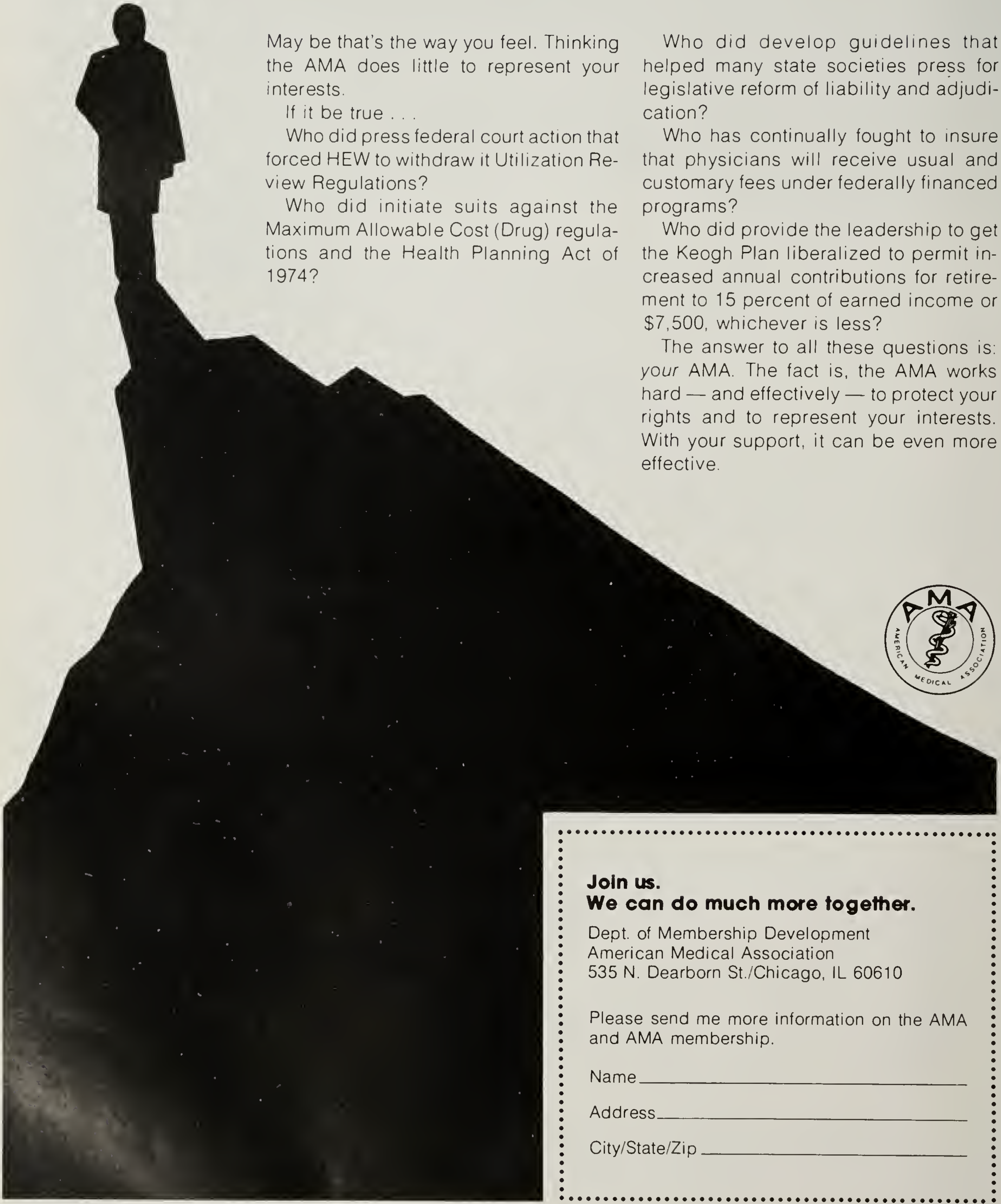

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Chronic Pain Patient Conquers Drug Dependence With Microceptor II Trancutaneous Nerve Stimulator

As the result of an industrial accident three years ago in which she suffered a brain concussion and compressed spinal column with nerve damage, Mrs. Phyllis Aeschlimann, Mesa housewife and mother of two 'teenagers, had such intense pain in her back, neck and right shoulder that she was bedridden. She had to be carried from room to room, and even minor activity was impossible.

Then, five months ago, after medication and physical therapy had failed, her doctor, an associate of the Pain Center of Mesa Lutheran Hospital, prescribed a Microceptor II Transcutaneous Electric Nerve Stimulator (TENS), a tiny, battery-powered instrument which blocks pain with electrical pulses transmitted through wires to soft, disc-shaped electrodes placed over pain control centers. Output is dialed up by the patient until pain disappears or becomes bearable.

Mrs. Aeschlimann reports: "After I got my Microceptor, improvement was gradual but steady. In six weeks, I could lead a nearly normal life. Today, I turn the current up only a third as far as in the beginning.

She also says that, although "the pill habit was hard to break," she now takes only three tranquilizers a *week*, rather than the 10 to 12 pain pills and six to eight tranquilizers per *day* she had been taking before.

Microceptors are not cure-alls, and are available only on doctor's prescription. However, in the many cases where they are effective, they provide these important benefits:

- **Reduction or elimination of dependence on drugs.**
- **No harmful side effects.**
- **Can be applied in 20 minutes by a doctor, nurse or physical therapist the first time, and by the patient thereafter.**
- **Unlike drugs, can be tried out without danger.**
- **Are approved by Medicare and most private health insurance policies.**

Now able to walk and take care of her home, Mrs. Phyllis Aeschilmann wears her Microceptor II out of sight on her waistband or brassiere. She is the founder of High Hopes of Arizona, Inc., a volunteer, non-profit organization for the rehabilitation of brain-damaged people.

Microceptor II is 2" wide by 3" long, weighs only 2.5 ounces. It is the smallest transcutaneous electrical nerve stimulator (TENS) made. Kit includes lead wires, electrodes and two interchangeable, rechargeable batteries.

CAUTION
U.S. federal law restricts this device to sale by or on the order of a physician.

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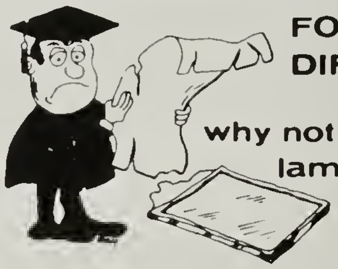

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***Usage in Pregnancy:* Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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The Maker

Examining a Few Myths About Prescribing.

Increasing pressure is being put on the practicing physician to prescribe drugs generically. You are told that brand–name products are universally “expensive” and generic versions are relatively “cheap.” To make this case, the most extreme (rather than typical) price differentials are cited. Thus, consumers are led to believe that such differentials are commonplace. Even your knowledge and your motives as a physician are questioned.

Understandably, these views have created myths. We think it’s time to examine them in the light of all the facts and ramifications.

MYTH: There are no differences in quality and performance between brand-name products and their generic counterparts. The corollary is that there are no differences among products made by high-technology, quality-conscious, research-based companies and those made by commodity-type suppliers.

FACT: The Food and Drug Administration does a good job in monitoring a generally excellent drug supply. Still, it has nowhere near the resources to guarantee the quality and bioavailability of all marketed products at any given time. Just a few months ago, for example, it noted that batches of tetracycline HCl capsules which met official monograph requirements were not bioequivalent to a reference product. As y know, there is substanti literature on this subjec affecting many drugs, i cluding such antibiotic as tetracycline and erythromycin. The record drug recalls and court actions affirms strongl that there are difference among pharmaceutical companies and their products. Research-intensive companies have far better records than those that do no re search and may practic minimum quality assur ance.

MYTH: Industry favors only “expensive” brand names and denigrates all generics.

FACT: PMA companies make 90 to 95 percent the drug supply, including, therefore, most of t generics. Drug nomenclature is not the impor tant point; it’s the comp tence of the manufacturer and the integrity the product that count.

Matters.

MYTH: Generic options almost always exist.

FACT: About 55 percent of prescription drug expenditure is for single-source drugs. This means, of course, that for only 45 percent of such expenditure, is a generic prescribing option available.

MYTH: Generic prescriptions are filled with inexpensive generics, thus saving consumers large sums of money.

FACT: Market data show that you invariably prescribe—and pharmacists dispense—both brand and generically labeled products from known and trusted sources, in the best interest of patients. In most cases the patient receives a proven brand product. Savings from voluntary or mandated generic prescribing are grossly exaggerated.

MYTH: Drugs account for a major portion of the rise in health care costs.

FACT: Drugs represent a very small part of such costs. The amount of the health care dollar spent for prescription drugs was about 12 cents in 1967; today it is about 8 cents. And you as a physician are most conscious of how drug therapy can cut hospitalization, avert surgery, reduce office visits and keep patients on the job.

MYTH: Government intrusions into the marketplace will save tax money.

FACT: Government schemes always cost the taxpayer something, and the costs often exceed the benefits. Certainly, any federal "help," such as lists of wholesale drug prices sent to all physicians and pharmacists, will be no exception. Just think of the expense of keeping them current! Moreover, wholesale prices are poor guides to actual transaction prices and even worse guides to retail prices.

The PMA Position

We believe your freedom to prescribe, either by generic or brand name, should be totally unabridged. Otherwise, your prescribing prerogatives and your relationships with patients will be seriously impaired.

The maker does matter

After the myths about price and equivalency have been shattered, one fact stands out more clearly than ever: *The maker does matter.* As always, your best guide to drug therapy for your patients is to select products—both brands and generics—from manufacturers with credentials and performance records you have come to respect.

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Tenuate Dospan®
(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION
Brief Summary

INDICATION: Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

WARNINGS: If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence.* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

ADVERSE REACTIONS: *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

DOSAGE AND ADMINISTRATION: Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in midevening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

OVERDOSAGE: Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

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References: 1. Citations available on request — Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'Dillon, R.H., and Leyland, H.M. A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy. Jan. 20-21, 1977.

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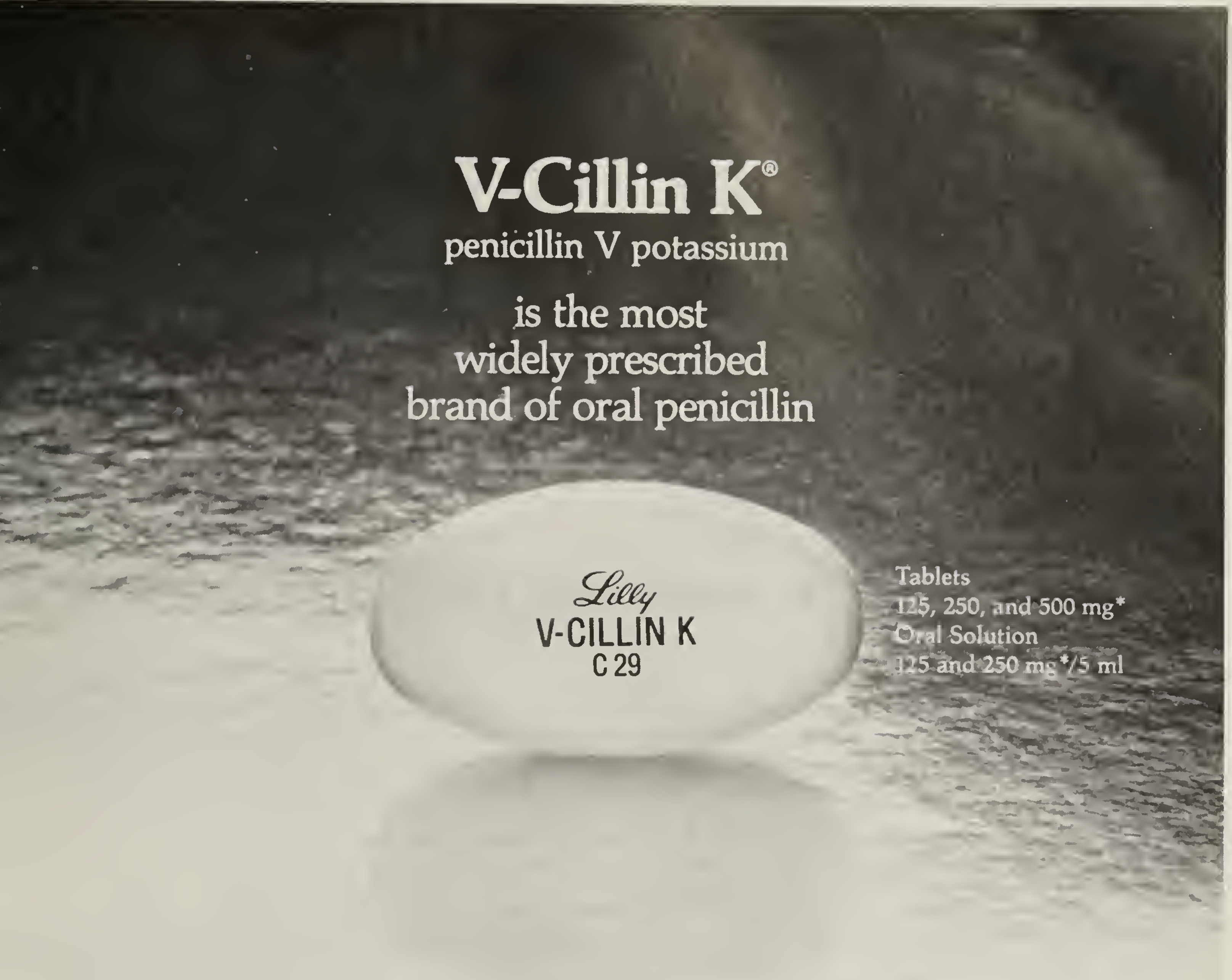

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Warnings: Serious, occasionally fatal, anaphylactoid reactions have been reported. Some patients with penicillin hypersensitivity have had severe reactions to a cephalosporin; inquire about penicillin, cephalosporin, or other allergies before treatment. If an allergic reaction occurs, discontinue the drug and treat with the usual agents (e.g., epinephrine or other pressor amines, antihistamines, or corticosteroids).

Precautions: Use with caution in individuals with histories of significant allergies and/or asthma. Do not rely on oral administration in patients with severe illness, nausea, vomiting, gastric dilatation, cardiospasm, or intestinal hypermotility. Occasional patients will not absorb therapeutic amounts given orally. In streptococcal infections, treat until the organism is eliminated (minimum of ten days). With prolonged use, nonsusceptible organisms, including fungi, may overgrow; treat superinfection appropriately.

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THE CHICAGO DEPARTMENT OF HEALTH

NEWS LETTER

VOL. 18, NO. 1, MAY, 1978

AUTOMATIC BLOOD PRESSURE DEVICES

A Chicago Department of Health report on the Vita-Stat automated blood pressure machines concludes that their consistency and accuracy is sufficient for screening purposes.

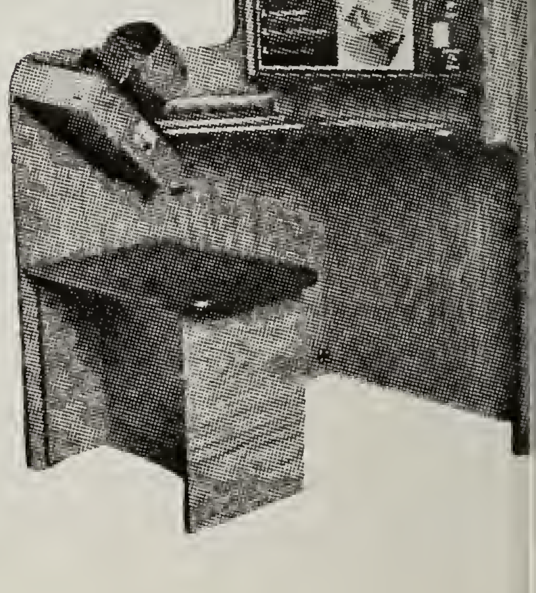
The report, the first in the nation based on a scientific study by a public agency, was prepared under the direction of Dr. David M. Berkson, the Department's heart disease control officer. It consists of (1) a statistical evaluation by Drs. Shekelle and Raynor of Rush-Presbyterian St. Luke's Medical Center, based on data collected over a four month period by Lawrence Shireman and Thomas Whipple and their co-workers in the Health Department, and (2) an evaluation of the results with recommendations for regulatory actions if deemed necessary. The report notes at the outset that any assessment of automatic blood pressure devices must compare their measurements with measurements by trained observers recorded by the traditional cuff ausculatory method. Since blood pressure may vary rapidly, the assessment of accuracy of measurement is difficult.

"In our evaluation of the Vita-Stat machine," the report states, "we found that, when the machine and a trained observer measure blood pressure simultaneously, there is a very good agreement." It is essential, however, that a machine must perform well in sequential measurement with trained observers as well as in simultaneous measurement. In sequential measurement the machine, in general, has a fair degree of accuracy. It does not perform as well, however, as trained technicians. In the laboratory analysis of the comparison between one machine and several technicians the machine tended to read systolic pressure 3.4mm higher and diastolic pressure 2.3mm lower. In the field analysis the machine tended to read systolic blood pressure 1.5mm and diastolic pressure 0.5mm higher than the technicians.

Although agreement between technicians in mean blood pressure measurement and in categorizing persons as normal, borderline or hypertensive tends to be closer than technician-machine agreement, these differences are small and of little practical significance in screening.

The report recommends that if licensing is insituted by the City of Chicago, periodic recalibration and testing should be required. The public must be informed that these instruments serve merely as screening devices; that they do not replace medical consultation and that, because blood pressure is subject to variation, several elevations or lack of elevations do not constitute a diagnosis of hypertension or normotension.

Blood pressure readings must be interpreted by a qualified medical professional and self-adjustment of medication based on automated blood pressure readings without medical supervision may be dangerous. The report concludes "that although the Vita-Stat machine does not perform as well as trained technicians, its consistency and accuracy is sufficient for screening purposes."



Value of Electrophysiological Studies In the Evaluation and Managment of Patients with Disorders of AV Conduction and Sinus Node Function

Dietmar Gann, M.D.
Jose Fernandez, M.D.
Lee Schocket, M.D.

His bundle electrocardiography was introduced into clinical practice ten years ago.[1] Its value as a diagnostic tool is undisputed; its use as an aid in the daily management of patients is less accepted. On the following pages we discuss the possible application of electrophysiological studies in the selection of patients with atrioventricular conduction and sinus node disorders who are given permanent pacemakers. Electrophysiological studies are only recommended in those patients in whom thorough clinical evaluation including 24-hour monitoring fails to clarify the indications for or against permanent pacing.

The PR segment of the surface electrocardiogram can be subdivided into three intervals with the help of His bundle recording (Figure 1). The PA interval measures conduction time from the sinus node to the low right atrium (normal up to 40 msec); the AH interval measures conduction through the AV node (normal 55-120 msec); and the HV interval measures conduction from the main His bundle to the ventricular muscle (normal 35-55 msec). A normal PR interval does not exclude prolongation in any one of the three segments, and a prolonged PR interval can be secondary to conduction delay in any or all of the segments. Block of conduction can occur in the PA, AH or HV segments.

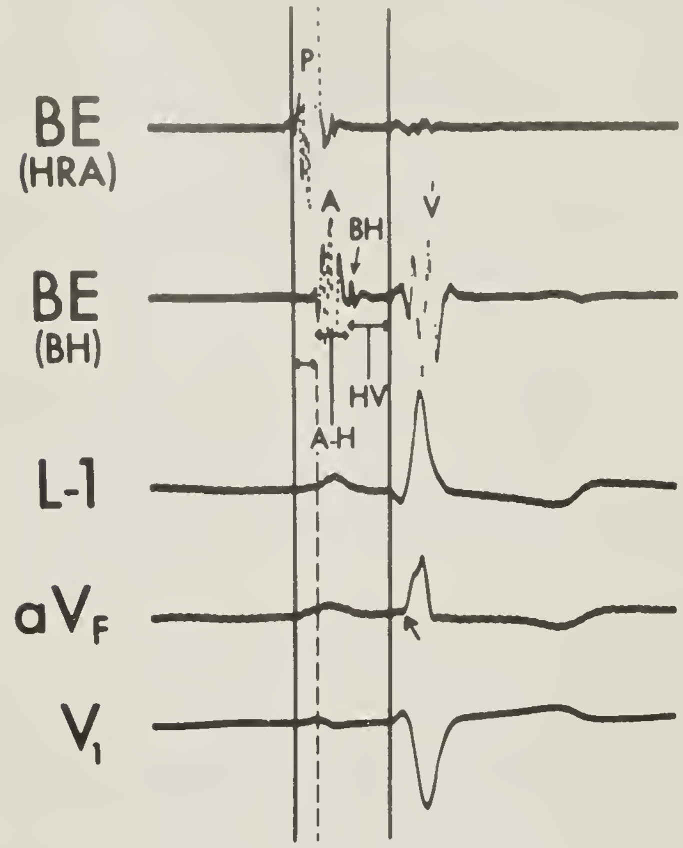


Figure 1
Typical His bundle recording. Three ECG leads (L1, aVF, V1) are taken simultaneously with recordings from the high right atrium (HRA) and bundle of His (BH).
BE: Bipolar electrogram

Atrioventricular Block:

Atrioventricular blocks (AV blocks) can be classified into first, second and third-degree blocks based on the PR interval of the surface electrocardiogram. In first degree AV block the PR interval is longer than 0.20 seconds. Second degree block is divided into two groups:

A. Mobitz type I or Wenckebach (Figure 2) - the PR interval progressively increases until a P wave is blocked.

B. Mobitz type II - the PR interval is constant and intermittently P waves are not conducted.

In third degree AV block no P waves are conducted. When most of the P waves are blocked and only occasional ones are conducted, the term "high-degree" AV block is used.

His bundle recordings have shown that first, second and third-degree AV block occur in the AV node, His bundle, bundle branches and Purkinje network[2] (Figure 3). First and second-degree AV block have also been described in the atrium. Blocks in the atrium or AV node are called supraHis (block occurs above the His bundle spike); blocks in the main His bundle are called intraHis (the His bundle spike is either prolonged (longer than 0.20 seconds) or split) and blocks occurring below the His spike are called infraHis. There is suggestive evidence in the literature that patients with intra and infraHis block should be permanently paced.[3, 4, 5] This is

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From: 5402 E. Grant Rd., Tucson, AZ 85712. Reprint requests to Dr. Gann.

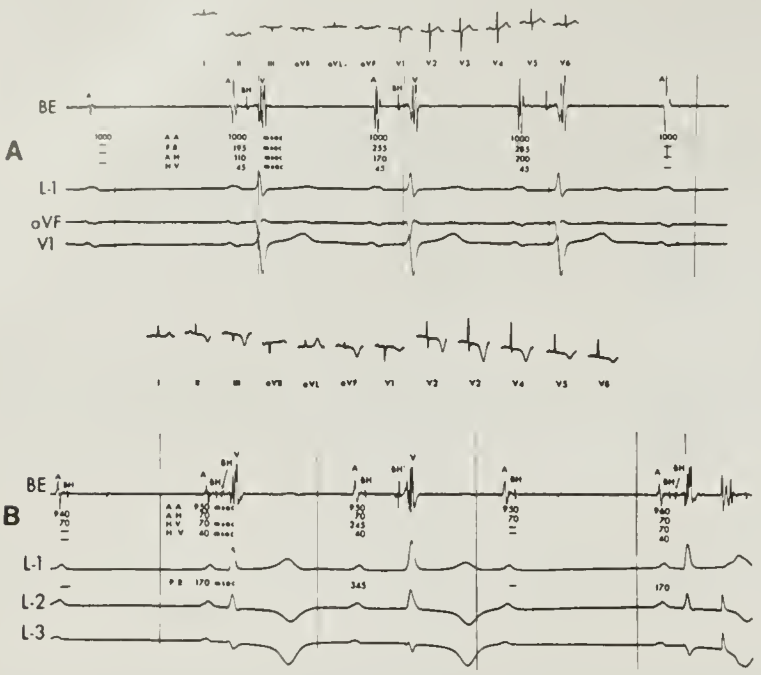

Figure 2
Two examples of second-degree AV block of the Wenckebach type with narrow QRS:
A. Block is located within the AV node. The blocked P wave is not followed by a His bundle deflection.
B. Progressive lengthening of the PR interval is due to a splitting of the His potential (BH and BH[1]). Block finally occurs distal to the first BH deflection.

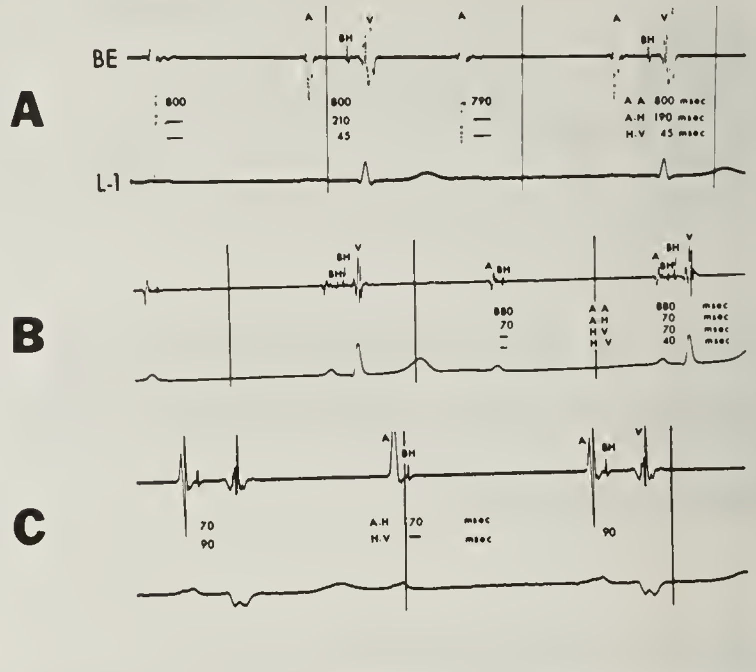

Figure 3
Three examples of 2:1 AV block:
A. Block in the AV node. Conducted beats show prolonged AH intervals of 210 msec. Atrial deflection is not followed by His deflection when P waves are blocked.
B. Block within the main His bundle. Split His bundle potentials are recorded during conducted beats (BH and BH[1]). P waves are blocked distal to the first His bundle spike.
C. Block distal to the main His bundle. HV time is prolonged (90 msec) during conduction. P waves are blocked distal to BH.

the justification for performing conduction studies in patients with AV block in whom we cannot confidently predict from the surface electrocardiogram where the block is located.

SupraHis blocks usually occur in the AV node and are considered relatively benign. The AH interval is either prolonged or block occurs after the A spike on the His bundle electrogram. This block is commonly associated with digitalis intoxication, inferior wall myocardial infarction, congenital heart block or is seen in healthy athletes due to excessive vagotonia. Second-degree AV block in supraHis block is usually of the Mobitz I type. In complete supraHis block the escape pacemaker is usually located in the main His bundle, is fairly reliable, usually faster than 40/min and responds to some degree to atropine and exercise.

IntraHis blocks are uncommon. They occur in 14 to 17% of patients with chronic complete heart block,[6,7] most of them elderly women. The QRS complex remains narrow if no additional bundle branch block occurs. In second-degree intraHis block Mobitz type I or II patterns are seen on the surface electrocardiogram. The escape pacemaker in complete intraHis block either originates in the lower His bundle or bundle branches, often is unreliable and slow.

InfraHis blocks are frequently due to sclerodegenerative disease or acute myocardial infarction. Second-degree AV block is usually of the Mobitz II type and in complete heart block the escape pacemaker has a wide QRS, is slow and unreliable.

Management of patients with AV block depends primarily on the clinical picture and findings on a regular electrocardiogram. All *symptomatic* patients with symptoms such as syncope, dizziness, congestive heart failure and low cardiac output should be paced if symptoms are thought to be related to a slow heart rate. No other studies are needed. Also, if heart rates persistently remain below 40/min even if the patient is asymptomatic, we usually pace the patient, because his course is unpredictable. In *asymptomatic* patients we try to predict the site of the block (supra, infra or intraHis) from either the heart rate, QRS duration or associated clinical picture and only in patients in whom the site of the block cannot be predicted do we proceed with conduction studies.

Patients with complete heart block, narrow or wide QRS complex and rate over 50/min in all likelihood have supraHis block and if asymptomatic should be observed only. At rates from 40-50/min no definate prediction of the site of the block can be made and conduction studies may be helpful. We suggest pacing only for those patients with block below the AV node, although we recongnize that other physicians will pace their patients regardless of the site of the block.

Demonstration of a *Mobitz type II* block almost always implies either intra or infraHis lesions. These patients are at risk for Stokes-Adams attacks or sudden death and we permanently pace all of them.[4, 5]

Patients with *Mobitz type I* block or Wenckebach block form a nonhomogeneous group. The block may be located in any region of the AV conduction system, regardless of the QRS width.[8]

The clinical picture gives the important information. If the Mobitz type I block is associated with digitalis toxicity, inferior wall myocardial infarction, or strenuous prolonged exercise in a young adult, then the block is usually located in the AV node and usually no permanent therapy is required. If the clinical picture does not help in locating the block, conduction studies may become useful.

Intraventricular Conduction Defects:

Rosenbaum popularized the concept of fascicular blocks.[9,10] Unifascicular blocks are right bundle branch block (RBBB), left anterior hemiblock (LAH), left posterior hemiblock (LPH). Left bundle branch block (LBBB), or right bundle branch block with either left anterior hemiblock or left posterior hemiblock (RBBB with LAH, RBBB with LPH) are bifascicular blocks. Complete interruption of all three fascicles results in trifascicular block or complete heart block. Many patients with chronic complete heart block were found to have precedent bifascicular disease.[11,12,13]

However, predicting which patient with bifascicular disease has impending complete heart block on the basis of the electrocardiogram alone is impossible. The reported incidence of progression to complete heart block from bifascicular block varies widely.[11,14,15]

After the introduction of His bundle studies it was hoped that there would now be a reliable test to be used in predicting which patient with bifascicular block would develop AV block in the near future. It was found that patients who had bifascicular disease with a normal third fascicle and normal His bundle would demonstrate normal HV times.[16] Therefore, a prolonged HV time in patients with bifascicular disease indicated additional disease in the remaining intraventricular conduction system, suggesting a higher likelihood of progressive AV block (Figure 4). Several studies subsequently showed that a prolonged HV time longer than 70 msec was associated with an increased risk of sudden death or the development of high-degree AV block.[17-21] However, others have differed with these findings.[22-24] Possible explanation for the differences in these studies are variability of symptoms, age and cardiac disease. Taking these variable findings into consideration, we suggest that *asymptomatic* patients with intraventricular conduction defects do not require any conduction studies, especially if they are under age 70 and have no asssociated heart disease.

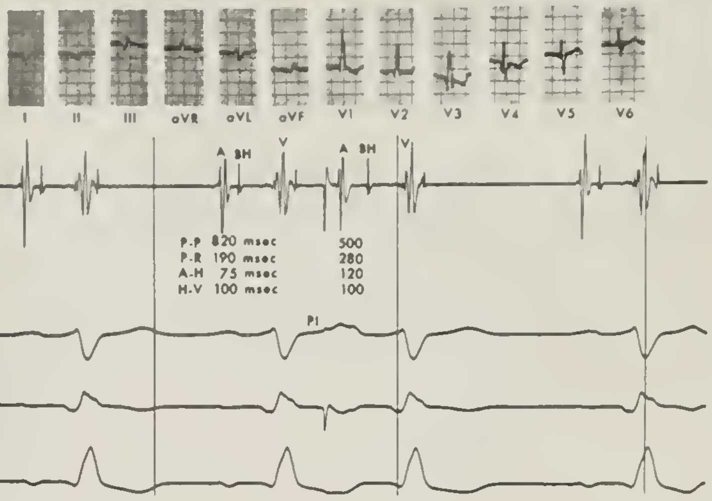

Figure 4
60-year old patient with right bundle branch block and right axis deviation, no known heart disease, recurrent syncope. Twenty-four hour monitoring was normal. His bundle recording reveals markedly prolonged HV time of 100 msec. Patient became asymptomatic after permanent pacing.

No uniformly accepted approach exists to patients with intraventricular conducton defects and symptoms such as syncope or dizziness in whom a thorough medical evaluation including 24-hour monitoring, did not reveal a cause of symptoms. Not uncommonly, patients with His-Purkinje system disease may exhibit complete heart block at one time and then continue to have 1:1 conduction again for days, weeks, or even months. Therefore, 24-hour monitoring after a Stokes-Adams attack may not show any conduction abnormality. Some physicians permanently pace these patients with the assumption that the patient probably has intermittent AV block and periods of asystole producing the symptoms. There is, however, evidence in the literature that this approach may not be correct and that measurement of the HV time may be helpful in deciding which patient to pace. Studies of patients with bifascicular block and transient complete heart block, or Mobitz type II block documented that a very high percentage of patients studied during 1:1 antegrade conduction exhibited prolonged HV times.[25,26] These findings suggest that a prolonged HV time is almost a necessary prerequisite for the development of complete heart block, and therefore a normal HV time in patients with syncope and bifascicular disease would almost exclude intermittent AV block as the cause of symptoms. In two studies, patients with bifascicular disease, syncope and/or dizziness and a normal HV time were not paced permanently.[17,21] None of the patients died suddenly or progressed to AV block over followup periods of 21 and 36 months, respectively. Therefore, in this very select group of patients with bifascicular disease and syncope or dizziness, His bundle studies may be helpful in avoiding pacemaker implantation.

Sick Sinus Syndrome:

The sick sinus syndrome encompasses sinus bradycardia, sinus arrest, sinoatrial block and the tachycardia-bradycardia syndrome.[27-29] Major symptoms are dizziness, syncope, weakness or less commonly congestive heart failure.

Twenty-four hour monitoring is the most useful test in the initial evaluation of patients with the sick sinus syndrome.[30] Only when continuous monitoring does not clarify the diagnosis and a sick sinus syndrome is still considered the cause of symptoms is additional testing necessary.

The most consistent electrical test of the sinus node is the *sinus node recovery time*.[31] In this procedure the atrium is paced through a pacemaker catheter at a rate of 80-150 beats per minute for a period of two minutes, then pacing is abruptly terminated. The time between the last

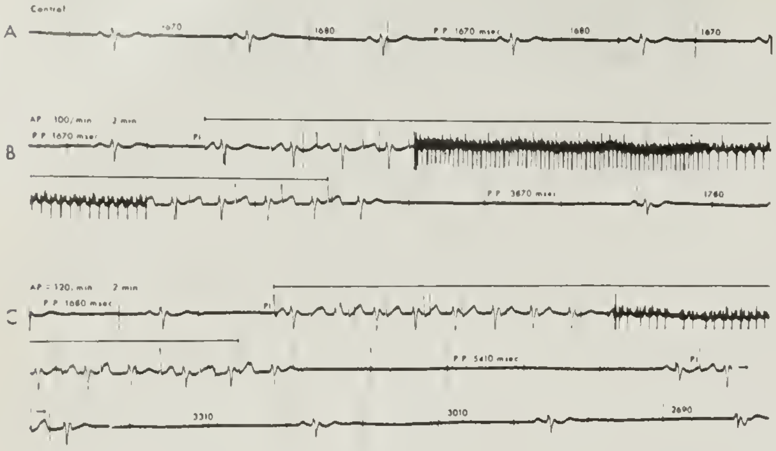

Figure 5

Typical example of an abnormal sinus node recovery time:

A. Basic cycle length 1670 mesec.

B. Sinus node recovery time after two minutes of atrial pacing at rates of 100/min equals 3879 msec. Corrected sinus node recovery time is 3870-1670= 2200 msec, markedly abnormal.

C. Sinus node recovery time becomes even more prolonged after atrial pacing at rates of 120/min.

paced beat and the first sinus beat is the sinus node recovery time. Deducting the basic P-P interval from the sinus node recovery time results in the *corrected sinus node recovery time* (normal 100-525 msec)[32] (Figure 5). Other tests, such as the response to atropine, measurement of the sinoatrial conduction time, evaluation of the first ten beats after atrial pacing is stopped, or checking the basic intrinsic heart rate after paralysis of the sympathetic and parasympathetic system with propanolol and atropine, may be helpful in selected patients.[33-35]

The sinus node recovery time is a highly specific test, but only 66% sensitive. Ninety-six percent of patients with a prolonged sinus node recovery time, sinus bradycardia and dizziness or syncope become asymptomatic after an implantation of a permanent pacemaker.[36] Therefore, a positive test strongly suggests that presenting symptoms are related to a diseased sinus node. A negative test including the additional ones mentioned above, does not completely exclude the possibility of a significantly diseased sinus node. However, patients with the sick sinus syndrome rarely die or suffer irreversible damage during recurring symptomatic episodes.[31, 36] Additionally, approximately 50% of patients with unexplained syncope or dizziness have no recurrent symptoms at all. Therefore, we believe it is acceptable to observe patients with unexplained syncope or dizziness if a thorough evaluation including electrophysiological studies remains negative. Permanent pacing should only be recommended if a relationship between symptoms and a diseased sinus node can be established.

Comments

No fixed guidelines exist on the indications for permanent pacing. In the United States more than ten times as many pacemakers per million population were inserted in 1975 as compared to England.[37] Broader diagnostic indications in this country and a less aggressive attitude of British physicians towards the subject of pacemaker therapy may be the reasons for this difference. Permanent pacing is expensive. The expenses were estimated in one study at 110 dollars per month for the life of the patient.[38] The use of a tool such as electrophysiology, which helps improve selection of patients for permanent pacing and potentially avoids unnecessary implantation is therefore justified.

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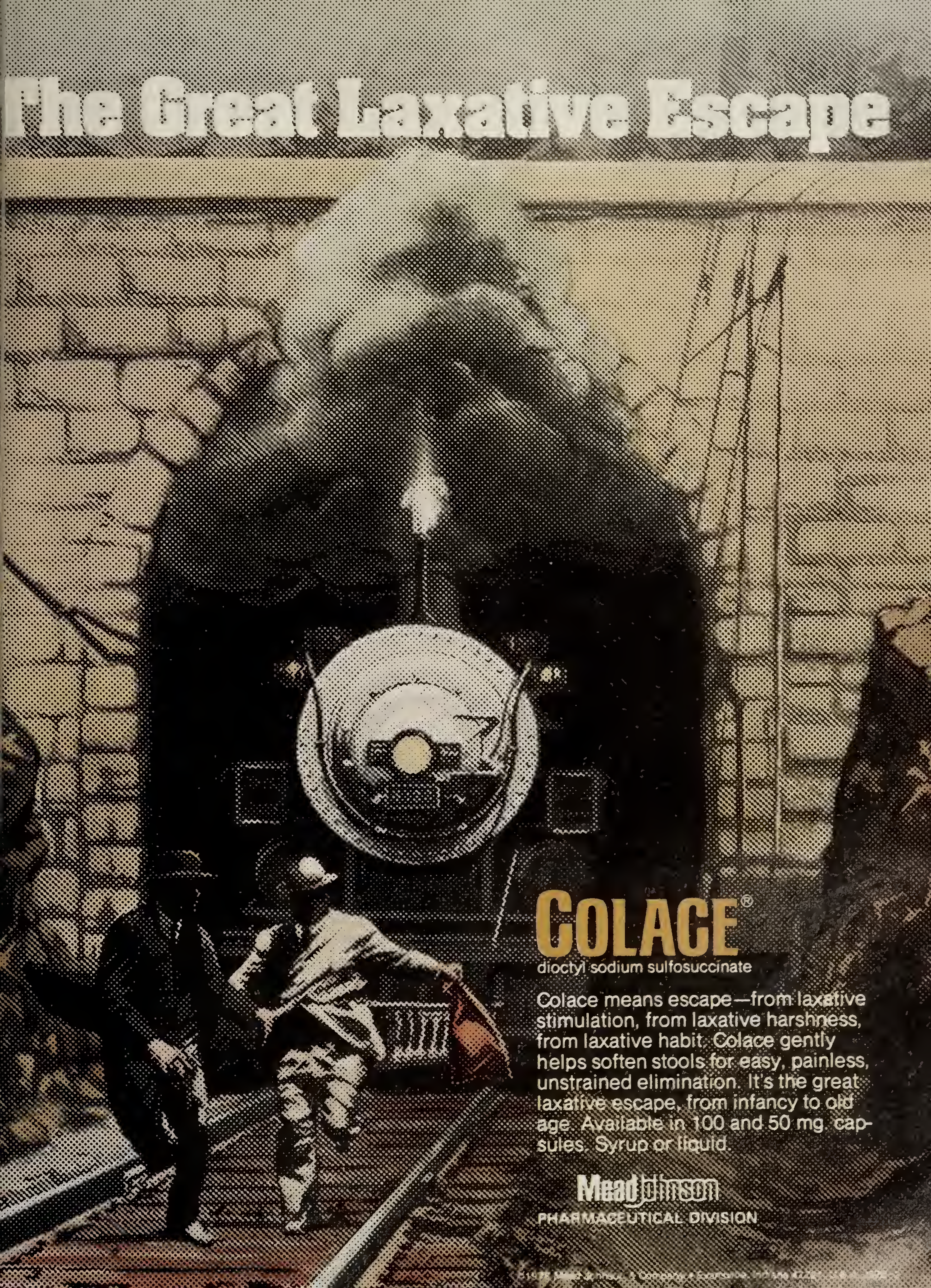

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Parenteral administration is not recommended in the presence of hypotension or tachycardia.

Intravenous administration should not be given because of increased likelihood of side effects.

Adverse Reactions: On rare occasions oral administration of the drug has been associated in time with the occurrence of hypotension, tachycardia, nausea, vomiting, dizziness, abdominal distress, and severe rash. If rash appears the drug should be discontinued.

Although available evidence suggests a temporal association of these reactions with isoxsuprine, a causal relationship can be neither confirmed nor refuted.

Administration of single dose of 10 mg. intramuscularly may result in hypotension and tachycardia. These symptoms are more pronounced in higher doses. For these reasons single intramuscular doses exceeding 10 mg. are not recommended. Repeated administration of 5 to 10 mg. intramuscularly at suitable intervals may be employed.

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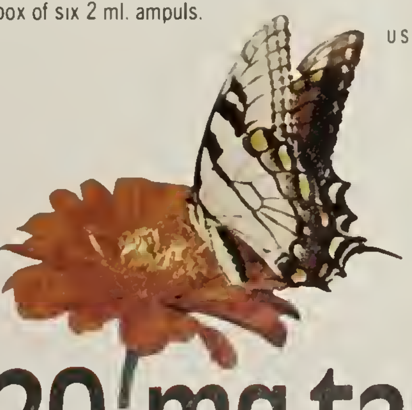

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Seminars in Chest Medicine

Lung Needle Biopsy

Jean-Paul Bierny, M.D.

I wish to report our experience in Tucson with the first one hundred (100) lung needle biopsies performed between October 1976 and March 1978 at Tucson Medical Center (89 patients), St. Joseph's and St. Mary's Hospitals. The procedure was performed with a new type of needle that provides excellent tissue for histological diagnosis and a very low complication rate.

Technique

A coagulation profile (PT, PTT, platelet count) is done preoperatively on those patients who have not had surgery without bleeding in the last 3 months. The needle [Figure 1] is an 18 gauge, 16 inch long Franseen

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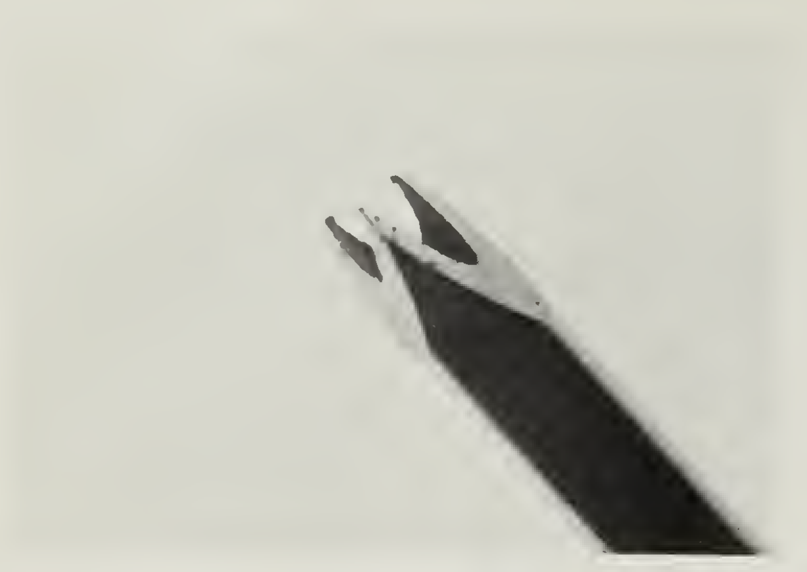


Figure 1

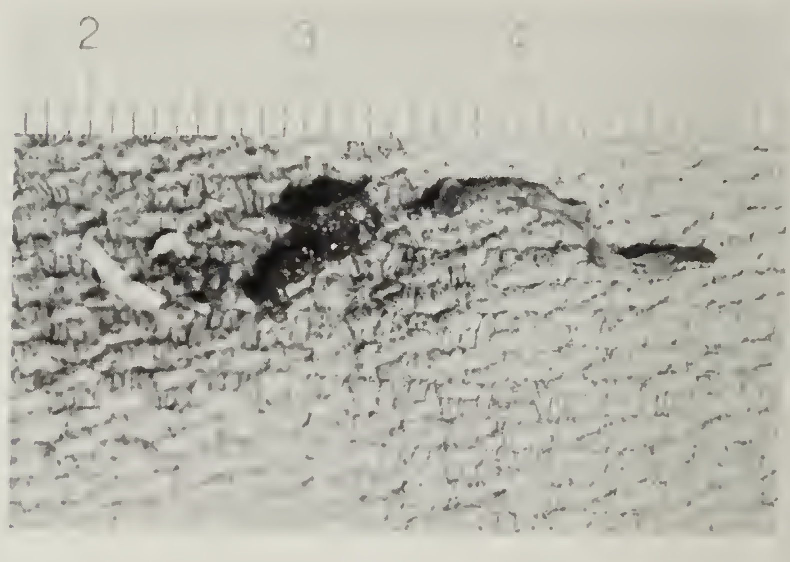


Figure 2

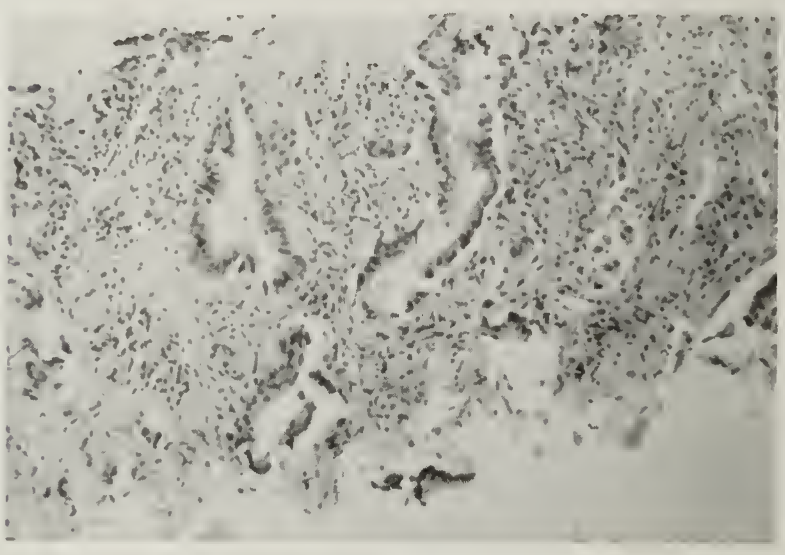


Figure 3

aspiration needle modified by Boyd[1] to have three bevels and thus three short cutting teeth. The procedure is performed under local anesthesia and vertical fluoroscopic control, and under constant suction. A 16 gauge Jelco needle is used to make a single thrust through the pleura. Its metal insert is then removed, and the plastic sleeve left in place as a guide for the biopsy needle. At the end of the procedure, a patch of the patient's own clotted venous blood is injected through the Jelco sleeve as the latter is withdrawn, thereby sealing the single pleural pulmonary tract.[2] The specimen is collected in a heparinized trap interposed between the extension tube connected to the needle and the wall suction tubing. Care has to be taken not to go through a pleural fissure with the biopsy needle, to avoid causing an additional pleural hole and increasing the risk of pneumothorax. Thus, the exact location of the lesion in relationship to the fissures must be assessed preoperatively on a lateral chest film or lateral tomograms, to decide whether the needle must be inserted through the anterior or posterior wall, in supine or in prone position. The patient is kept in the x-ray department for one hour after the end of the procedure, and chest x-rays are taken immediately after the procedure and one hour later to check whether a pneumothorax is developing. The patient comes back for a last chest x-ray on the next morning for further safety. The specimen is a core of tissue [Figure 2] usually eminently fit for histological diagnosis. Cultures are routinely taken for AFB, fungi, bacteria.

Indications

Circumscribed lung masses of any size or location (96 patients), and localized or diffuse alveolar or interstitial lung infiltrates (4 cases). Needle biopsies in hilar areas are done only after unsuccessful biopsy attempt through bronchoscopy.

Contraindications

Bullous emphysema along the needle path increases considerably the chances of causing pneumothorax. Pulmonary hydatid cysts, or vascular masses. Positive histology by bronchoscopic biopsy, or positive smear or culture for AFB, fungi. Uremia and pulmonary hypertension warrant prior consultation with the referring physician because of the increase risk of bleeding.

Results

A pathological diagnosis was obtained from 89 out of the 100 patients, including seven biopsies done twice. Sixty-seven were malignant, (22 adenocarcinomas [Figure 3], 22 squamous cell carcinomas [Figure 4], 18 undifferentiated carcinomas [6 large cell and 12 small cell,] 5 metastatic carcinomas). Thirty-nine of these patients had surgery, which confirmed the histological diagnosis in each case and 32 had chemotherapy, radiation therapy, or no treatment. Twenty-two patients had benign conditions, including 10 cocci, (seven with cocci spherules in addition to caseous inflammatory granuloma [Figure 5,] and three had only positive cocci cultures from necrotic material,) seven had other nonspecific inflammatory conditions (one of these had Group III atypical Mycobacteria associated with achalasia,) and 5 had miscellanea (nodular amyloidosis,

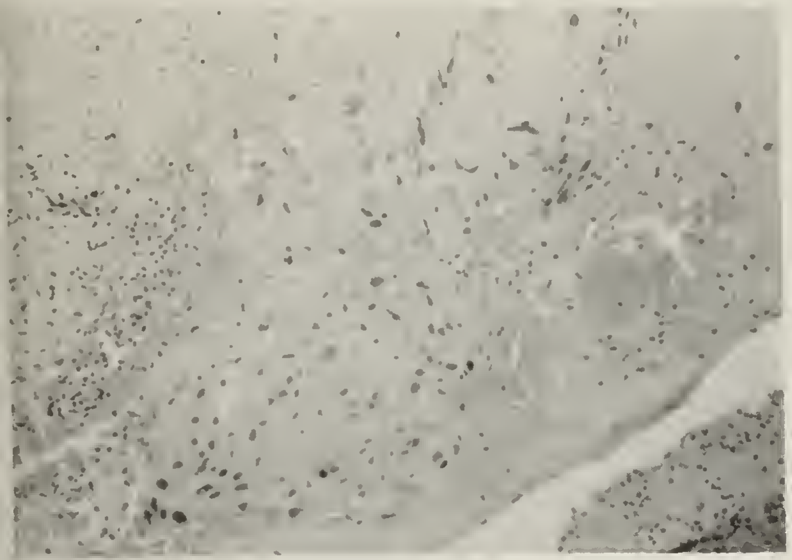


Figure 4

Figure 5

benign chondroma, anthracosis, bleomycin reaction, leiomyomatosis). None of these 22 patients underwent surgery. Eleven biopsies yielded nondiagnostic tissue: fibrosis, necrosis, blood. Two of these went to surgery and had cancer. There were no false positives for cancer.

Seven patients were biopsied twice; at the second biopsy, three showed cancer, two cocci, one atypia, one was nondiagnostic. Out of the 96 mass lesions, 32 were of 2cm. or less in diameter (out of which 25 were diagnosed by lung needle biopsies) and 64 were larger than 2 cm. (out of which 59 were diagnosed by biopsy). Twenty-two of the cancer patients underwent bronchoscopy with biopsy prior to the needle biopsy—two of these had a positive cytology (considered as strongly suggestive, but not quite diagnostic of CA, unlike histology).

Complications

Seven patients showed a small asymptomatic pneumothorax. Four patients had a significant pneumothorax which required a chest tube. One of these had severe emphysema, and another one had leukemia, and the quality of the blood patch injected through the needle at the end of the procedure was poor. A few patients had hemoptysis, of no clinical significance.

Discussion

The high diagnostic yield of 89% (including the 7 biopsies done twice), is felt to result mainly from the ease of pathological diagnosis on the frequently excellent core of tissue obtained, as opposed to techniques using very thin aspiration needles that yield only cytological specimens. Our yield is comparable to those obtained at the Cleveland Clinic[3] or at the Loma Linda University.[1] The procedure affords rapid resolution of the diagnostic problem frequently raised by lung masses of inflammatory, or malignant etiology (primary or metastatic). In the case of cancer, it also indicates usually the cell type, which is quite important to help distinguish between primary or metastatic malignancy, to plan further work-up or therapy. This applies particularly in the case of undifferentiated, small cell carcinomas, which are unlikely to benefit from surgical resection. However, it was at times difficult for the pathologist to distinguish between primary and secondary disease (from breast or gastrointestinal tract for instance) when dealing with an adenocarcinoma. The same problem is encountered during surgical resection of small peripheral lesions, since their exact spot of origin from bronchial mucosa is often exceedingly difficult to pinpoint. The problem of origin of a metastatic lesion can at times be solved quite rapidly by a needle biopsy, avoiding an otherwise potentially long and costly search for a primary, or settling the question of origin in patients with multiple primary cancers. In a patient with a history of previous cancer of the uterus and malignant fibrous histiocytoma for instance, the lung needle biopsy showed that the lung metastasis originated from the fibrous histiocytoma [Figure 6]. In another one, with a previous cancer of the breast and another one from the colon, the lung needle biopsy showed tissue similar to the breast primary.

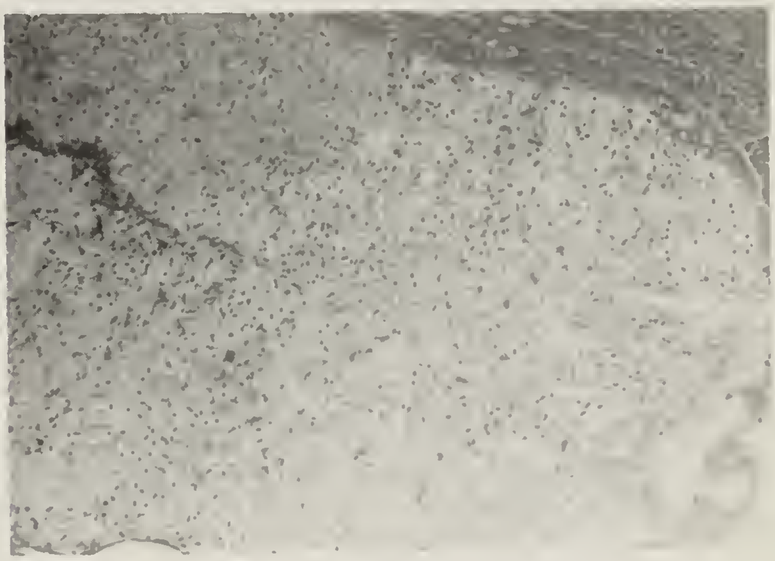


Figure 6

The easy diagnosis of cocci by lung needle biopsy of lung nodules is, of course, very interesting in Arizona. These granulomas, being interstitial and often subpleural, would be very difficult to approach by

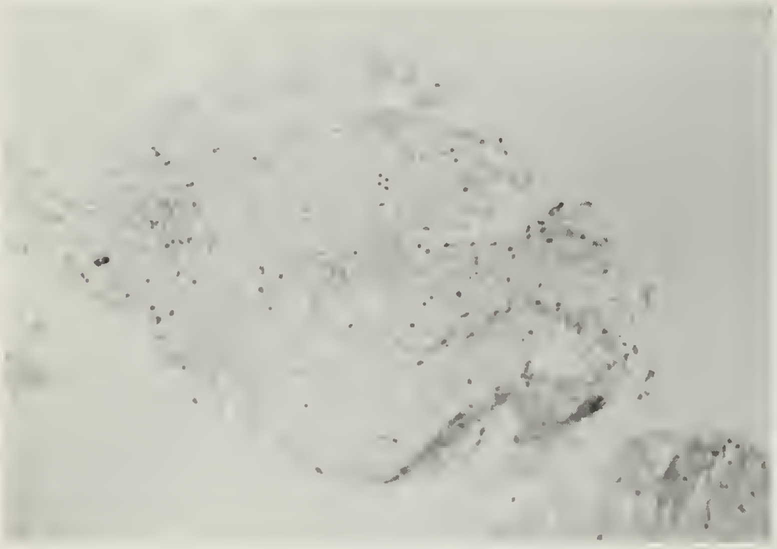
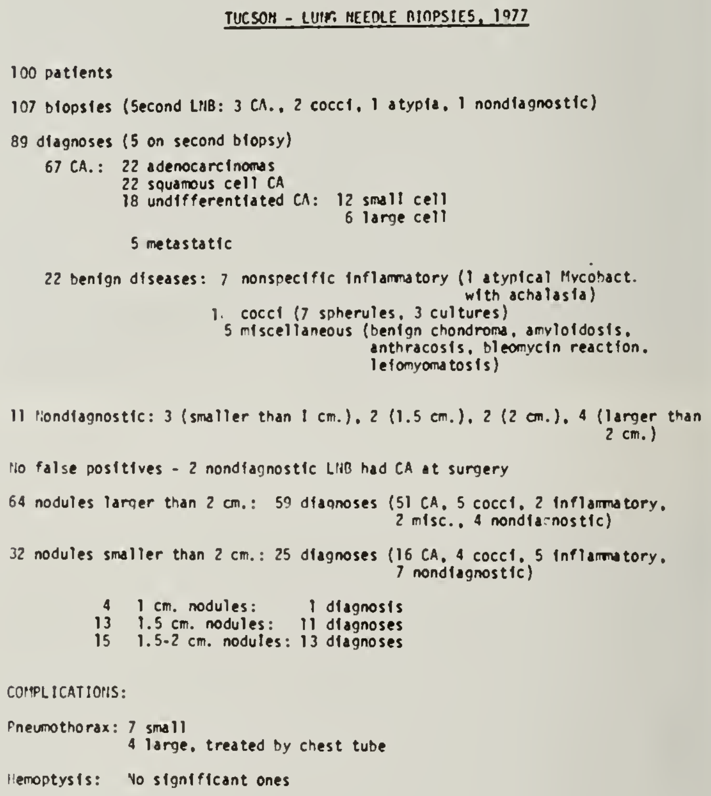


Figure 7

Figure 8

transbronchial route. Rarely, their hard consistency makes them difficult to transfix with the needle. The exact etiological organism of the other seven inflammatory lesions could not be established (except one case), but at least malignancy was ruled out by the lung needle biopsy. It was interesting to find out that benign non-inflammatory lesions could also benefit from lung needle biopsy. A 40 year old man with a 4 x 3 cm right upper lobe mass turned out on lung needle biopsy to have benign chondroma, [Figure 7] and thus did not undergo surgery. A leukemic patient who developed extensive lung infiltrates, felt to be probably infectious, showed no acute inflammatory diease, but only an inflammatory pattern compatible with reaction to the bleomycin treatment that she was undergoing. A 50 year old man with multiple sizeable lung nodules discovered on a routine preoperative chest x-ray for inguinal hernia, and suspected to represent multiple lung metastases, underwent lung needle biopsy, which showed primary nodular amyloidosis of the lung [Figure 8]. This represented a very significant short-cut in a work-up that could have been quite lengthy and expensive in a search for a primary carcinoma. It is felt that the procedure is underused for lung infiltrates, which represent less obvious indications for the clinician. Lesions such as lymphangitic spread of tumor, disseminated cocci, collagen disease, tuberculosis, sarcoidosis, pneumoconiosis, lipoid pneumonia, pneumocystis carinii, have been diagnosed in this fashion. The low complication rate results from the use of a single pleural hole, the constant wall suction, and especially, the injection of the blood patch through the needle as it is pulled out. Because of the safety of the procedure, it was performed as frequently as possible as an out-patient procedure, provided that the medicosocial circumstances permitted it.

Cocci skin tests were positive, and cocci serology, performed in most, were negative on all 17 patients whose lung needle biopsy showed cocci or other inflammatory lesions. These tests were thus remarkably unhelpful.



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                    TUCSON - LUNG NEEDLE BIOPSIES, 1977

100 patients

107 biopsies (Second LNB: 3 CA., 2 cocci, 1 atypia, 1 nondiagnostic)

89 diagnoses (5 on second biopsy)
    67 CA.:  22 adenocarcinomas
             22 squamous cell CA
             18 undifferentiated CA:  12 small cell
                                       6 large cell

              5 metastatic

    22 benign diseases:  7  nonspecific inflammatory (1 atypical Mycobact.
                                                      with achalasia)
                        10  cocci (7 spherules, 3 cultures)
                         5 miscellaneous (benign chondroma, amyloidosis,
                                          anthracosis, bleomycin reaction,
                                          leiomyomatosis)


11 Nondiagnostic: 3 (smaller than 1 cm.), 2 (1.5 cm.), 2 (2 cm.), 4 (larger than
                                                                      2 cm.)

No false positives - 2 nondiagnostic LNB had CA at surgery

64 nodules larger than 2 cm.:  59 diagnoses (51 CA, 5 cocci, 2 inflammatory,
                                             2 misc., 4 nondiagnostic)

32 nodules smaller than 2 cm.: 25 diagnoses (16 CA, 4 cocci, 5 inflammatory,
                                             7 nondiagnostic)

           4   1 cm. nodules:      1 diagnosis
          13   1.5 cm. nodules:   11 diagnoses
          15   1.5-2 cm. nodules: 13 diagnoses


COMPLICATIONS:

Pneumothorax: 7 small
              4 large, treated by chest tube

Hemoptysis:   No significant ones
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Figure 9

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Seminars in Endocrinology and Metabolism

Oral Hypoglycemic Agents

To Use or not to Use That is the Question

Stephen E. Dippe, M.D., F.A.C.P.

Diabetes mellitus was treated only with insulin and diet until the discovery that sulfonylureas* lowered blood glucose levels in the 1950's. Since sulfonylureas are taken orally, it allowed some patients to stop taking insulin injections and for others to be less strict on their dietary control. Thus, sulfonylureas became a major mode of therapy of the treatment of maturity onset diabetes. In 1959 a study was begun to determine whether or not keeping the blood glucose level controlled would prevent the vascular complications in the diabetic patient. The study was restricted to those who had maturity onset diabetes that did not require insulin to control their disease. The study became known as the University Group Diabetes Program (UGDP) and has three main objectives:[1]

1. Evaluation of the efficacy of hypoglycemic treatments in the prevention of vascular complications in long term, prospective and cooperative clinical trial.
2. Study on the natural history of vacular disease in maturity onset, non-insulin dependent diabetics.
3. Development of methods applicable to cooperative clinical trials.

The main objective of this study, then was not to determine if oral hypoglycemic agents were effective in controlling blood glucose levels, but to see if the control of blood glucose levels would reduce the vascular complications in a specific diabetic population. The study was divided into four seperate treatment groups.

1. Variable insulin dose - These patients received as much insulin as necessary to maintain a normal blood glucose with minimum value being five units per day.
2. Standard insulin dose - Ten to 16 units of Lente Insulin were given daily depending on the patients body surface.
3. Tolbutamide (Orinase) dose - 1.5 grams of tolbutamide (Orinase) was given daily with 1 gram before breakfast and 0.5 grams before the evening meal.
4. Placebo - The Placebo correspondent to the oral hypoglycemic agents in use.

From: Family Practice Center, Scottsdale Memorial Hospital, 7301 E. 4th St., Scottsdale, AZ 85251

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*Example: tolbutamide (Orinase), acetohexamid (Dymelor), tolazamide (Tolinase) and chlorpropamide (Diabinase).

Phenformin (DBI) was added later to the study but will not be discussed in this paper.

Since the results of the study were made available in 1970, there has been considerable controversy as to the accuracy of its conclusion.[2] The results stated simply suggest that persons who took the oral hypoglycemic agent tolbutamide (Orinase) suffered a higher frequency of cardiovascular deaths than did any of the other treatment groups. It was concluded that tolbutamide (Orinase) was the agent responsible for the increased cardiovascular death rate.

Almost as soon as the results of the study were known, there were numerous articles, statements, meetings, arguments, debates, etc. concerning the value of the study. Due to conflicting reports, many physicians were confused about the value of oral hypoglycemic agents in the treatment of diabetes. Many physicians made their own conclusions and either prescribed or did not prescribe oral hypoglycemic agents, as there was a lack of consensus in the community of diabetic experts. The public also became involved with this study and has left patients opinionated or skeptical about the treatment of diabetes making the physician's job more difficult.

Since the inception of the study and the release of its conclusions, much as been learned about maturity onset diabetes; such as the effect of obesity. Obesity plays a role in the development of maturity onset diabetes. Thus, dietary restriction and weight loss have become the major thrust in the treatment of mild maturity-onset diabetes not drugs. Often times with weight control alone, normalization of mild carbohydrate intolerance is possible. In the UGDP study, many of the patients were obese and apparently adequate dietary control was not complete. In addition, there was little attempt to control the blood glucose level in the UGDP study subjects except those in the variable dose insulin treated group. Careful control of the blood glucose level may indeed affect the microvascular system favorable.[3] There appears no doubt that certain factors play a predominate role in cardiovascular disease such as hyperlipoproteinemia, hypertension and cigarette smoking. There apeared to be little, if any, control of these potential risk factors in UGDP study.

It should be emphasized that the UGDP protocal used only one sulfonylurea, tolbutamide (Orinase), in a fixed daily dose.

A conclusion not related to tolbutamide (Orinase) in the UGDP study may be in error. The UGDP study reported no difference in the cardiovascular death rate between the placebo treated group and the variable insulin dose treated group. However, Dr. Kilo and his associates[4] reanalyzed the UGDP data and concluded that the variable insulin dose treated group has a lower cardiovascular death rate than the placebo group. They concluded that insulin treatment is efficacious in reducing cardiovascular death rate. This finding would support the concept that better diabetic control results in a better effect on the cardiovascular system (macrovascular system). As far as the microvascular system (retenopathy and nephropathy) is concerned, good control of diabetes does have a favorable effect. In support of good control, the American Diabetes Association issued the following statement: "Current clinical and experimental data clearly demonstrate that optimal regulation of glucose levels should be achieved in the treatment of diabetes, particularly in young and middle-aged individuals who are at greatest risk of developing the microvascular complication."[3] Hopefully, by obtaining as good a control as possible in the diabetes, it will result in an improved and prolonged life by reducing both the microvascular and macrovascular.

Obviously, many factors must be considered besides the level of blood glucose in order to determine the type of treatment and the degree of control needed. The physician must consider such things as the patient's age, occupation, work hours and the patient's mental, physical and emotional status. Consideration has to be given to the degree of compliance the patient is willing to accept. Evaluation of his determination and motivation towards tight control is essential. Also, his level of knowledge, about diabetes and its acute complications, such as hypoglycemia, must be examined. It's also important to obtain an honest appraisal of the patients willingness to adhere to the treatment prescribed to him. In some patients, tight control may cause deterioration in their social, economic and emotional stability. Thus, many factors enter into the treatment of a diabetic and all must be considered before determining the type of treatment, as well as the degree of their control.

Thus, when all factors are considered it's up to the physician to decide what type of therapy should be used. The oral hypoglycemic agent should not be used indiscriminately but only after careful evaluation of the patient and his disease. The current view of the American Diabetes Association states:[5]"The patient - physician interaction should continue to be the primary area of decision-making regarding the appropriate therapy for the individual diabetic patient whether that therapy is diet alone, diet plus insulin, or diet plus oral sulfonylurea." Well put.

Supported in part by the Edyth Bush Charitable Foundation, Inc.

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Seminars in
Gastroenterology
and Liver Disease

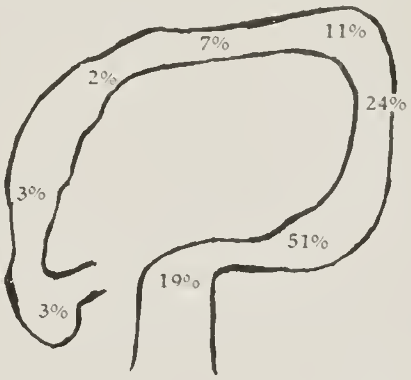
Polyps of the Colon

Stephen Glouberman, M.D.

Editors:
Leon Rigberg, M.D.
Stephen Glouberman, M.D.
George Burdick, M.D.

A polyp of the colon is defined as an epithelial lesion which projects into the lumen. This definition excludes such lesions as lipomas and leiomyomas, as these are tumors that originate in the submucosa. There are three types of polyps. *Hyperplastic* polyps are nonneoplastic. They are usually small, of the same color as the surrounding mucosa, and are comprised of enlarged epithelial cells. They have no malignant potential and will not be discussed further. *Adenomatous* polyps are the most prevalent type of neoplastic growth. They vary in size from a few millimeters to several centimeters, are frequently pedunculated, and are characterized by proliferation of cells forming a nodule of well-differentiated glands of large bowel type, and may produce mucus. They have enlongated, crowded, hyperchromatic nuclei. Their malignant potential will be discussed subsequently. *Villous* polyps are less common than the adenomatous variety, are often soft and pliable, and tend to be sessile, rather than peduculated. Histologically, they consist of proliferated goblet cells which take on a frond-like pattern. The production of large quantities of mucus or fluid may be associated with some of the larger ones.

The incidence of polyps varies with the method used for detecting them. In barium enema studies, polyps are present in up to 19% of individuals so examined. Autopsy series have shown polyps to be present in up to 39% of patients. The distribution of polyps tends to be throughout the colon, with a predominance on the left side.[1]



Adenomatous Polyps

Adenomatous polyps are frequently incidental findings on barium enema, sigmoidoscopic or colonscopic examinations. They are usually clinically silent, but may be associated with abdominal cramping, a change in the patient's bowel pattern, rectal bleeding or mucus in the stools. Their size varies form 1-2 mm. up to 5-6 cm. or larger. Approximately 20% of patients have more than one polyp coexistent.[2] Seventy-five percent of all benign polyps are adenomas.

Several uncommon conditions are associated with the development of adenomatous polyps. *Familial polyposis* is an autosomal dominant condition in which the colon is studded with hundreds of polyps. They may appear at any age, but usually first appear in the teens. However, the development of polyps prior to age 10 has occured. The development of malignancy appears inevitable. Villous growths are sometimes seen. *Gardner's Syndrome* is also a genetically determined condition with autosomal dominant heredity. Adenomatous polyps of the colon are found in association with epidermal cysts, mesenchymal tumors, such as fibromas, lipomas and leiomyomas and bony tumors. The malignant potential

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From: 3411 North 5th Ave., Ste 503, Phoenix, AZ 85013.

of the colonic adenomas is considered as great as in familial polyposis. *The Turcot syndrome* is the association of colonic adenomas with central nervous system neoplasia. The colonic tumors are thought to be premalignant.

The diagnosis of a colonic polyp is usually first made by barium enema. A 23% false positive, and 54% false negative, rate has been reported for the routine barium enema examination.[3] A barium enema employing air-contrast has a 5% false positive, and 11.7% false negative rate.[4] A major factor in the false positive rate of detection of colonic polyps by the barium enema is inadequate preparaton of the patient. A well cleansed colon is mandatory for proper performance of this very important diagnostic test. The use of a liquid diet for two days, adequate cathartics on the day prior to the examination, and a cleansing enema on the morning of the study is essential if an adequate barium enema is to be performed and maximum information obtained from this study. Colonoscopy has been found to be more accurate for the detection of polyps, and adequate colonic cleansing is mandatory for this examination to be performed. This procedure is associated with a 2.7% false negative rate for detection of polyps (due to mucosal redundancy or a polyp hidden behind a flexure or mucosal fold), and 10% of polyps cannot be reached by the colonoscope.[4] In almost all instances, a barium enema precedes the colonoscopic examination.

In addition to the symptoms listed above, another major reason for the detection of polyps is their malignant potential. Of polyps less tha 1 cm. in size 1.3% are malignant. Of those between 1 and 2 cm. in size, 9.5% are malignant, and 46% contain cancer if the polyp is greater than 2 cm. in diameter.[2] For many years, it was thought that adenomatous polyps were not premalignant lesions, and that cancer arose de novo, not from one of these polyps.[5] It is now well established that this concept is not correct, and that innumberable examples exist of carcinoma existing within a adenomatous growth. Approximately 5% of all adenomas contain cancer.[2]

Villous Polyps

Ten percent of all colonic polyps are villous, and 15% contain features of both adenomas and villous tumors. About 3/4 are found within the reach of the sigmoidoscope. Eighty-nine percent are sessile, the remainder having stalks. Rectal prolapse on defecation has been reported with these tumors, especially with low-lying ones. They may secrete a large amount of mucus and electrolytes, sufficient to produce severe dehydration, electrolyte imbalance and uremia.[6]

Approximatley 40% of all villous tumors have a malignancy in them at the time of diagnosis.[2] Therefore, the malignant potential for this type of tumor is far grater than for the adenomas. The reason for this is unclear. The presence of a stalk does not protect against the malignant potential. If the polyp contains both adenomatous and villous features, then 22% will be malignant.[2]

Treatment

The treatment for adenomas should be removal, if at all possible. If the polyp can be reached by the sigmoidoscope, attempts should be made to remove it. If above the reach of that instrument, it is deemed preferable to attempt to remove the lesion via the colonoscope. Although the risk of malignancy is low in polyps less than one cm. in size cancer has been found in polyps as small as 3mm. If the patient is in good clinical condition, colonoscopy should be performed for total colonic evaluaiton. As stated earlier, 20% of patients have more than one polyp.[2] Furthermore, of coexisting polyps not seen by routine barium enema, 3% are malignant, and 66% are proximal to the splenic flexure.

Colonoscopy is not without risk. Approximately 1% of patients bleed following removal of a polyp, and perforation of the colon occurs in about 0.5% of examinations. About 12% of polyps are not removed by the colonoscope,[4] usually because of inability to reach them.

Laparotomy should be considered for removal of polyps not removed by the colonoscope. Since the malignant potential does not reach 2% for polyps until they are greater than 1 cm. in size, and the operative mortality for laparotomy is about 2%, this procedure should be reserved for those polyps which are greater than 1 cm. in size, not removed by the colonscope, and are present in a patient thought capable of tolerating the surgery. If the polyp is smaller than 1 cm and bleeding is present, laparotomy should again be considered if prior colonoscopy has been unsuccessful. The treatment of choice for familial polyposis and Gardner's syndrome is total colectomy.

Conclusion

In any individual with a polyp of the colon, careful follow-up is indicated by air-contrast barium enema and/or colonoscopy at periodic intervals. If a benign polyp is removed, there is a 4% likelihood that a colonic cancer will develop in 25 years. If a cancer is initially present, there is a 10% chance that a second cancer will develop in 25 years.[2] One acceptable follow-up program is a total colonoscopy performed one year after removal of a benign polyp and if negataive, an air-contrast barium enema and/or total colonoscopy performed every two years thereafter. The development of symptoms should result in more immediate investigation.

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Neurology

Neurologic Complications of Infectious Mononucleosis

Michael S. Smith, M.D.
Jose F. Laguna, M.D.

Editors:
Betty F. Ball, M.D.
Barry Hendlin, M.D.
Lawrence Z. Stern, M.D.

Infectious mononucleosis (IM) is a common, usually self-limited disease of young adults. While prolonged convalescence, hepatic involvement, and splenic rupture are well-known complications of IM, the plethora of neurologic complications are not as well recognized. We wish to report a case of Guillain-Barre syndrome secondary to IM and to review the neurologic complications of IM.

Case Report

A 21-year old electrician developed sore throat and malaise approximately a week prior to admission to the Morenci Hospital. Mono spot was positive and the patient was initially treated symptomatically.

Four days prior to that admission he noted tingling in both feet. Two days later, he had to leave work early because of fatigue while standing. The day of admission, he was unable to walk without help. He denied headache or stiff neck. Lumbar puncture performed at the time of the admission was acellular, with a normal opening pressure, a normal glucose, and a protein of 270 mg percent. The patient was transferred to the University of Arizona Health Sciences Center with a diagnosis of Guillain-Barre syndrome.

On arrival, the patient was unable to stand, anxious and tachypneic. He was alert, oriented in all spheres, and not dysarthric. Cranial nerves were normal except for a facial diparesis. Motor strength was 4/5 (Medical Research Council) in his upper extremities, 2/5 in his lower extremities. Coordination was normal in the upper extremities, taking into account the patient's weakness. Coordination in the lower extremities was unable to be evaluated adequately because of weakness. Sensation was initially intact to pinprick, vibration, position, and stereognosis. The patient was areflexic; plantar responses were flexor bilaterally.

Admitted to the medical intensive care unit, he developed profound weakness during the ensuing 72 hours. Elective tracheostomy was performed because of deteriorating vital capacity, and he was placed on a respirator. A week after his tracheostomy, he had reached the nadir of his illness, with complete paralysis of cranial nerves VII, IX, and X, 2/5 strength in his upper extremities, and complete paralysis of the lower extremities. His clinical course was complicated by tachycardia, labile hypertension, urinary retention, inappropriate ADH secretion and pneumonia which were vigorously treated.

He remained on the respirator for five weeks before he could begin to breathe by himself. Eight weeks after admission he was able to return to the referring hospital because of sustained improvement. Cranial nerves and arm strength had returned to normal, and he had 3/5

From: University of Arizona Health Sciences Center, Depart. of Neurology, Tucson AZ 85724. Reprint request to Dr. Smith.

residual weakness in his lower extremities. Epstein-Barr virus titers were 1:80 acute (ill for two weeks) and 1:320 convalescent.

Discussion

The incidence of serious neurological complications in IM has been reported to vary between 0.37 and 5.5 percent of cases.[1, 2] Most authors accept an incidence of one percent. The electroencephalogram, however, has been reported to be abnormal in 32 percent of cases and spinal fluid to be abnormal in 26.5 percent.[3] Besides Guillain-Barre syndrome, other neurological complications associated with IM are meningitis, encephalitis, mononeuritis, transverse myelitis, autonomic dysfunction, numerous ocular problems, and neuralgic amyotrophy.

Guillain-Barre syndrome in association with IM was first reported in 1942.[4] In the next thirty years, approximately forty additional cases were reported in the literature. This complication occurs about as often as meningitis or mononeuritis. These three complications together account for about one-third of the neurologic manifestations of IM. Guillain-Barre associated with IM may occur either before, during, or after the clinical onset of IM. It may also be the *only* manifestation of IM and is treated no differently than other forms of Guillain-Barre.

Encephalitis associated with IM was first described in 1931.[5] It is the most common neurologic manifestation of IM, accounting for more than half the cases. The encephalitis may present as a first seizure,[6] as confusion and disorientation, resembling herpes simplex encephalitis,[7] or as an acute cerebellar syndrome,[8, 9] with ataxia, dyssynergia, rebound, and hypotonia. Hemiplegia has also been reported.[10] The pathology of IM-associated encephalitis has not been well-studied, due to the generally good prognosis of the disorder. In the few fatalities that have come to autopsy, polioencephalitis, with large numbers of atypical cells in the exudate and in the parenchyma, has been described.[11] In addition, engorgement of vessels in the leptomeninges with petechial hemorrhages and perivascular hemorrhages has also been found.[12] In the acute cerebellar syndrome, Purkinje cell degeneration occurs.[8, 9] Nearly all patients with the cerebellar syndrome recover in three weeks to three months.

Mononeuritis may affect the facial nerve, either unilaterally[13] or bilaterally,[14] although the latter may simply represent a mild form of Guillain-Barre syndrome. Other cranial nerves which may be selectively affected include III, VI, IX and X, and XI.[15]

Transverse myelitis is a very rare complication of IM, only nine cases having been reported in the literature as of 1973.[16] The prognosis is not necessarily grave, and recovery may occur.

Yahr described acute autonomic neuropathy as a complication of IM.[17] His patient suffered syncope secondary to orthostatic hypotension, pupillary changes and bowel atony.

IM may affect the eye in numerous ways. Conjunctivitis, periorbital edema, and uveitis are primary ophthalmological manifestations. Ptosis, extraocular muscle palsy, nystagmus, and optic neuritis may also occur.[18]

Brachial plexus neuropathy (neuralgic amyotrophy, Parsonage-Turner syndrome) was first reported in 1943 by Saksena,[19] who described paralysis of the serratus anterior following IM. This type of neuropathy is an unusual complication of IM, only fifteen cases having been reported by 1976.[20]

The course of most of the neurological complications of IM tends to be benign, although deaths and prolonged disability are not uncommon. The key point is that numerous neurological syndromes may be the presenting form or a complication of IM. Therefore, any acute neurologic syndrome in a young person should prompt a search for IM as the cause. In the case of Guillain-Barre syndrome, proper management in an intensive care unit and attention to respiratory complications can be life-saving.

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Obstetrics and Gynecology

The Vagina: An Ecologic Challenge

Edward A. Friedrich, Jr., M.D.

Donald J. Ziehm, M.D., Editor

The vagina can be likened to a river - it has a flow, a river bed and an ecology. The river bed is the squames with all the microridges and glycogen characteristic of vaginal squamous epithelium. Nourished by glycogen, the normal flora reside within the microridges. The basal cells, under the influence of estrogen, develop into mature squames. The ecology: the patient with all the factors (especially the hormonal influences) that affect her. Glycogen is produced as the vaginal epithelium matures from basal to superficial cells. As a result of this growth, an autofermentation process occurs and acid is produced (Propionic acid, Acetic acid, Lactic acid). The flora is affected; very few bacteria can survive in an acid environment. Utilizing glycogen as a substrate the vaginal flora produce additional protective acidity, etc.

But the ecology can unwittingly be fouled up. Oral contraceptives and pregnancy both can significantly disturb the hormonal mileau. In both of these situations the amount of glycogen is increased; the acidity is modified and the flora affected. In another common example, the flora can be altered by well intentioned efforts to treat acne. Tetracycline is prescribed. As a result the normal flora is often destroyed and a Candida infection develops - totally predictable. Therefore, whenever an antibiotic is prescribed (especially Tetracycline) the patient should be protected for a possible Candida infection.

The acidity of the vagina may be influenced. Masters and Johnson's work demonstrated that intercourse is probably the most effective way to decrease the vaginal acidity. Immediately after ejaculation the vaginal pH rises from 3.5-4.0 up to 7.0. It remains at this elevated and abnormal level for a number of hours, returning to

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From: Dept. of Ob/Gyn, The Medical College of Wisconsin, Dr. Friedrich Associate Professor. Presented at "New Advances in Obstetrics and Gynecology," Phoenix, AZ, February 14, 1979.

normal in about 8 hours. Thus, the woman who has intercourse three times a day never has a normal pH in her vagina. How often do patients relate: "I only get the infection after intercourse; he must be giving it to me." The assumption is that the male is transmitting an infection. Not so. A dose of buffer is being administered in the semen. Semen must be alkaline for sperm to survive. Alkaline semen deposited in the vagina produces and alkaline vagina. And in some women that is just enough to distrub the ecology and allow normal flora to be replaced by pathogenic bacteria. A simple solution is to instruct the female to douche within 30 minutes after intercourse and thereby flush out the buffer. The nature of the douching solution probably doesn't make a great deal of difference; vinegar is cheap and easy to use. Another approach is to have the male use a condom. The former is more acceptable to most couples, but condoms will accomplish the same purpose as doucing - prevent the buffer from getting into the vagina and remaining there for long periods of time.

Effective management of vaginal infections requires accurate diagnosis. All that is needed is KOH solution, normal saline, some slides, a microscope, and *the willingness to use them*. Nitrazine paper is also helpful; it will change color in exactly the pH range of the vaginal secretions. If the vaginal pH is known the type of vaginitis can almost be predicted. With a pH between 3.5-4.0 (the normal range) primarily flora are present. Candida can exist and flourish at almost any pH; it's a very hardy organism. Thus the use of baking soda douches to counteract Candida found in an acid vagina is ineffective, since Candida will thrive just as well in an alkaline environment. As the pH rises, between 4.0 and 5.0, the normal flora decreases. Many types of pathogenic bacteria (which are always resident in the cervix) may proliferate. Hemophilis vaginitis is found in a pH between 5.0 and 6.0. If the pH is less than 5.0 don't bother looking for "clue cells." Trichomonas will prosper in an alkaline pH, moreso than most other organisms. Thus, listening to the patient's complaint, looking at the discharge, making a wet smear, and testing the vaginal pH will enable one to characterize vaginitis very quickly into 4 categories: Candida, Trichomonas, atrophic conditions, and "other" (primarily Hemophilis).

Candida: The branching, budding hyphae can be seen even with prolonged scanning, but that's all that is necessary. Most Candida infections are autoinfections, developing from the Candida present in the patient's own GI tract. Females who wipe from back to front may have recurrent Candida infections. Once they are taught to wipe from front to back the recurrences are much less frequent. So ask the patient that aspect of her personal hygiene when taking a gyn history. Oral Nystatin is helpful in patients with recurrent attacks. It should also be used to protect patients who must use Tetracycline or other systemic antibiotics. Gentian violet is an old, but a cheap and effective form, of therapy. When applying Gentian Violet to the vulva and vagina, remember to rotate the speculum so that all vaginal tissue is covered. Still another approach is painting the vagina with Gentian Violet followed by the use of Monistat or Gyne-lotrimin cream for one week. The process may be repeated if the infection is still present one week later. Rarely are more than 2 applications of Gentian Violet necessary. A group of gynecologists in California, interested in wine making, found that using Potassium Sorbate would destroy the yeast in their wine. They reasoned that it might possibly be effective for Candida; and so it was. In Wisconsin it is also effectively used to spray on cheeses to help retard the growth of mold. A 3% aqeous douch of Potassium Sorbate can be very helpful in controlling recurrent Candida infections. It's not terribly effective as a primary therapy, but may reduce the number of recurrences.

Trichomonas: All frothy, bubbly vaginal discharge is not Trichomonas. The vaginal pH is high, around 6.0. The motile Trichomonads are easily visulized in a hanging drop preparation with normal saline. A 50% error rate has been reported when using the Pap smear to diagnose Trichomonas. Flagyl remains the most effective treatment. The old dosage schedule was 250 mg tid X 7 days. But 500 mg bid for 5 days is just as effective and cheaper. Fairly good results may also be obtained with a 2 gram stat dose, although nausea may be a bothersome side effect. Remember that the patient should avoid alcohol ingestion when using Flagyl.

Atrophic Conditions: Occur with a lack of estrogen. Glycogen is absent because of failure of the vaginal epithelium to mature. Thus, the necessary acidity is absent. An alkaline pH exists, allowing numerous organisms to proliferate. Microscopic examination of an atrophic vaginitis reveals many pus cells in association with large parabasal cells. Unlike the large flat squames, parabasal cells have a high nuclear-cytoplasmic ratio. They are readily seen on the wet smear. Parabasal cells are typical of an atrophic vaginitis. This type of infection may frequently be present in children; a vaginal culture would probably grow coliform bacteria. Small amounts of feces-contaminated toilet paper can get behind the hymeneal ridge producing a presistent bacterial coliform type of vaginitis. The vagina can easily be flushed by gently directing a flow of normal saline from 250 cc bag toward the vulva and vagina. In effect this is a douche, but in a very non-traumatic way. Often many little bits of toilet paper will be flushed from the vagina in this manner. A small amount of Sulfa-containing estrogen cream can then be applied with a finger. The mother and child must also be educated in the hygenic measures necessary to prevent the vaginitis from recurring. Lactation is a similar atrophic situation. The woman who is breast feeding has an atrophic vagina. For this reason many women at this time will complain of painful intercourse. Prophylactic Premarin cream used during lactation will keep the vagina well estrogenized and protected. One-half an applicator once or twice a week is not enough estrogen to affect lactation.

Hemophilis: Characterized by a subtle gray, malodorous discharge. "Clue cells" (vaginal squames with clusters and colonies of coccobacillae on the surface) are diagnostic when seen on the wet smear. "Clue cells" are uniformly granular with fine, tiny granules. They can easily be mistaken for the squames with irregular , coarse and fine granules. The previous treatment of choice for Hemophilis vaginitis was Penicillin. However, recenty the administration of Cephradine 500 mg qid for 6 days has been found to be much more effective. Flagyl, used in the same dosage as for the treatment of Trichomonas, also seems to be quite effective.

Chlamydiae: May present as a persistent, purulent vaginitis and cervicitis. Culture techniques are currently available for confirming the diagnosis. Tetracycline 250-500 mg qid for 3-4 weeks often will clear this infection (remember to protect the patient from the possible development of a Candida vaginitis).

Herpes: Can affect the vagina as well as the external genitalia. The classical herpetic ulcers may/may not be seen. Herpetic cervicitis and vaginitis can be completely asymptomatic, being found only on a Pap smear. So the Pap smear should be routine in the workup for vulvovaginitis, even if a negative smear was recently obtained. Repeat it; you may find Herpes. If present, Betadine douches twice a day for a week is as effective as any other form of treatment.

Occasionally a patient may be encountered who presents with a persistent watery discharge with a pH about 5.0, a slight amount of mucus, some squames, but no WBC. Despite all attempts at diagnosis, no cause of the vaginitis can be found. If the patient is on oral contraceptives, could this discharge represent a sort of hydrorrhea gravidarum? Seen frequently in pregnancy, it may develop secondary to the pseudopregnancy induced by oral contraceptives. If the discharge begins with the onset of use of birth control pills and stops when oral contraceptives are discontinued, the patient may have to consider the use of another form of contraception.

A significant amount of vaginitis may be on an emotional basis. "I've got pain in the vagina;" "I've got a vaginitis." In some patients with these complaints no cure can be achieved despite multiple and heroic attempts at diagnosis and treatment. The complaints persist. Consider the possibility of an underlying marital, sexual or emotional distress. Gentle questioning may elicit many previously unrecognized emotional problems.

Finally, the telephone is not a diagnostic or therapeutic instrument. When a patient seems to be resistant to all therapy and continues to call, ask her to come in for a vaginal smear. An infection different from the last one diagnosed may be present. Try to resist the temptation of using the phone for diagnosis and treatment.

Oncology

Current Concepts in the Management of Gestational Trophoblastic Disease

Thomas N. Suciu, M.D.

Editor:
David Alberts, M.D.

Introduction

Gestational trophoblastic disease encompasses a spectrum of disease processes ranging from benign to highly malignant. Prior to the introduction of chemotherapy into the treatment of this entity, the survival rate for patients was usually poor.[1,2] However, in 1956 a patient with metastatic choriocarcinoma was successfully treated with chemotherapy, ushering in a new era in the treatment of trophoblastic disease.[3] Numerous studies published in rapid succession resulted in the following conclusions:[4,5,6] First, a significant number of these patients can be cured with chemotherapy. Second, higher cure rates and less therapy are associated with early detection of this disease. Third, the toxic side effects of chemotherapeutic agents are predictable and rarely fatal if the person administering them is experienced with their use and adequate laboratory expertise is available. Finally, less than adequate therapy often results in subsequent development of resistant disease.[7] Refinements to these conclusions have subsequently led to the excellent overall survival rates which now exist.

Although appropriate and aggressive initial therapy has resulted in much higher cure rates for patients with gestational trophoblastic neoplasms (GTN), the development of sensitive and accurate laboratory measurements of human chorionic gonadotropin (HCG) has been of equal importance in this regard. In fact, it can be said that one cannot properly treat or follow patients with GTN without such an assay. The beta sub-unit radioimmunoassay[8] is the test currently in use at the Southwestern Regional Trophoblastic Disease Center.* Other quantitative determinations of HCG may be used to follow patients if positive. However, once the HCG level has fallen below the detectable limits of these tests,

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From: Dept. of Obstetrics and Gynecology, University of Arizona Health Sciences Center, 1501 N. Campbell Ave., Tucson, AZ 85724

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*Southwestern Regional Trophoblastic Disease Center, Dept. of Obstetrics and Gynecology, Gynecologic Oncology Section, University of Arizona Health Sciences Center, Tucson, AZ 85724.

Table 1
Clinical Classification
Of Trophoblastic Disease

1) Hydatidiform Mole
2) Non-Metastatic Gestational Trophoblastic Neoplasia (NMGTN)
3) Metastatic Gestational Trophoblastic Neoplasia (MGTN)
    (a) good prognosis
    (b) poor prognosis

the beta sub-unit assay is used. Several different criteria for determining "negative" results may be employed by the laboratory and one should be familiar with his laboratory's reporting criteria and type of assay.

The clinical classification of GTN may be divided into three categories which are used to determine appropriate treatment (Table 1). Metastatic disease may be further subdivided into good- and poor-prognosis categories. Metastatic, poor-prognosis disease is distinguished by any of the following criteria: 1) initial urine HCG titer greater than 100,000 international units per 24 hours, 2) metastasis to the brain or liver, 3) duration of symptoms greater than 4 months, 4) disease that has failed to respond to significant previous chemotherapy,[9] 5) disease occurring after a term pregnancy.[10] It is particularly important that this group of metastatic, poor-prognosis patients be treated initially with aggressive therapy if optimal remission rates are to be achieved.

Benign Trophoblastic Disease

The hydatidiform mole is characterized by cystic swelling of the chorionic villae and is associated with an intact fetus less than 5% of the time. The microscopic appearance is characterized by edematous villae, loss of vascular pattern, and varying degrees of trophoblastic proliferation. There is marked geographic variation in the incidence of molar pregnancies. It is estimated to occur in approximately 1 in 2,000 pregnancies in the United States, with a tenfold increase in Mexico. Some 50% of patients with metastatic GTN and 75% of patients with GTN without metastasis initially had molar pregnancies.

Table 2
Signs and Symptoms of Molar Pregnancy
(Frequency of Occurrence)

Bleeding in first half of pregnancy	(90%)
Lower abdominal pain	(30%)
Toxemia prior to 24 weeks gestation	(30%)
Hyperemesis gravidarum	(15%)
Uterus large for date	(50%)
Absent fetal heart tones and fetal parts	(95%)
Theca-lutein cysts	(30%)
Thyrotoxicosis	(2%)

The signs and symptoms of a molar pregnancy are shown on Table 2. Quantitative HCG determinations may be helpful in the diagnosis and are generally elevated above 500,000 international units per liter in patients with molar pregnancies. If the diagnosis of hydatidiform mole is suspected, confirmation may be obtained with ultrasound studies or amniography. Once the diagnosis has been established, the uterus should be emptied as soon as possible. Suction evacuation has the lowest complication rate of the methods currently available to the practitioner and therefore should be the procedure of choice when available. Mechanisms involving the induction of labor, such as oxytocin or vaginal prostaglandin E2 suppositories, may increase the incidence of major blood loss, infection, and trophoblastic pulmonary embolization and often a D & C is required to complete the uterine evacuation.[11,12] Hysterectomy with mole *in situ* is an acceptable alternative to suction evacuation in those patients requesting sterilization and may reduce the subsequent incidence of malignant sequelae.[7] It should be pointed out, however, that hysterectomy does not eliminate the necessity for careful follow-up and HCG testing. Hysterotomy and intrauterine injections of hypertonic solutions should be avoided, if possible, as it appears that these two methods of evacuation have excessively high complication rates. Other factors which may complicate the treatment of molar pregnancies include: anemia, toxemia, hyperthyroidism, high output cardiac failure, abortion with hemorrhage and/or sepsis, and trophoblastic pulmonary embolization. Having had one molar pregnancy, a patient is at a four- to fivefold increased risk for subsequent molar pregnancies. Additionally, 10% - 20% of patients having molar pregnancies will have proliferative sequelae requiring further treatment.[13,14]

Our current recommendations for follow-up of patients with hydatidiform mole include a pre-evacuation chest x-ray which is repeated 2 — 4 weeks after evacuation. Frequent follow-up pelvic examinations are performed to ensure that uterine involution is occurring and that there is regression of any cystic ovarian enlargement, as well as cessation of vaginal bleeding. HCG levels are determined at 1 — 2-week intervals until three consecutive negative beta sub-unit radioimmunoassays are obtained. Pregnancy testing is useful only when positive.[15] Once the beta sub-unit HCG titer has fallen to undetectable levels, the assay is repeated at 1 — 2-month intervals for 1 year. We have found that repeated curettage is of no assistance in follow-up or management of these patients, and the potential for major complications exists should perforation occur through locally invasive uterine tumor. The decision to treat a patient in the post-molar surveillance period is based on the appearance of metastatic lesions, a plateaued or rising HCG titer, a re-elevation of HCG titer after reaching normal pituitary levels, or a histologic diagnosis of choriocarcinoma. Adequate contraception should be utilized during the post-mole surveillance period and it is suggested that patients not attempt pregnancy until 1 year of negative follow-up has been achieved.

The Southwestern Regional Trophoblastic Disease Center is currently not recommending the routine use of "prophylactic chemotherapy" in patients having molar pregnancies evacuated. Although most of the data available on the use of "prophylactic chemotherapy" indicates that there is a reduction in the incidence of post-molar proliferative complications, other evidence suggests that the overall mortality may be higher in the prophylactically treated group.[16] The basis for this may be partially related to the development of resistant disease. Additionally, since only 10%— 20% of patients with molar pregnancies will develop proliferative complications, prophylaxis would entail treating 80% - 90% of patients unnecessarily. Finally, current methods of evaluation permit early detection of those post-molar pregnancy patients who need further treatment and therefore essentially 100% of these patients will be curable provided careful follow-up is performed.[9]

Malignant Trophoblastic Disease

The spectrum of disease in the category of GTN includes malignancies under the pathologic terms of hydatidiform mole (after initial evacuation), invasive mole (chorioadenoma destruens), and choriocarcinoma. All of these conditions are preceded by some type of pregnancy and over 50% of patients initially had molar gestations. The diagnosis may be more difficult in patients in whom the disease follows a non-molar pregnancy because of the wide diversity in presenting symptoms and the failure to include trophoblastic disease in the differential diagnosis.[17] It should also be remembered that commercial pregnancy testing may be negative in as many as 30% of these patients.[15]

Once the decision to treat has been reached, a thorough diagnostic workup should be done. We determine the initial HCG titer and, after history and physical examination, stage the patient with chest x-ray, computerized tomography or isotopic liver and brain scan, electroencephalogram, intravenous pyelogram, and complete assessment of bone marrow, liver, and kidney function. On occasion, D & C, pelvic ultrasound, tomography, or arteriography may be indicated. On the basis of these results, the patient may be placed into one of the categories of disease shown in Table 1 and appropriate therapy may then be selected.

Non-Metastatic Trophoblastic Disease

Most of the patients with initial disease confined to the uterus will be those with careful follow-up after molar pregnancy evacuation. The patient and physician should come to a decision as to whether preservation of further reproductive ability is desired. We then initiate single-agent chemotherapy utilizing either methotrexate or actinomycin D. as shown in Table 3. If hysterectomy is contemplated, we prefer to perform this on the third day of the first 5-day course of chemotherapy. Lewis and others have reported no increased post-surgical morbidity in patients receiving these agents who were submitted to a variety of surgical procedures.[18] Chemotherapy should be continued in the post-surgical period until HCG levels are undetectable to prevent the growth of tumor which has either been disseminated during the procedure or which was present and unidentified at the time of surgery. Repetitive courses of the same drug are given until the HCG titer reaches normal pituitary ranges for 3 consecutive weeks. The patient may then be followed in the same fashion as the postmolar-evacuation patient.

Table 3
Single-Agent Chemotherapy Protocol

1) Methotrexate: 0.4 mgm/kg/day I.M. for 5 days (maximum single dose, 25 mgm)
OR
Actinomycin D: 10-13 micrograms/kg/day I.V. for 5 days (maximum single dose, 750 micrograms)
2) Repeat courses with 7-day minimum interval provided:
    (a) toxicity clearing
    (b) WBC greater than 3000/mm^3, granulocyte count greater than 1500/mm^3, and platelet count greater than 100,000/mm^3
    (c) normal hepatic and renal function
3) Weekly HCG titer until within normal pituitary range for 3 consecutive weeks.
4) Follow-up HCG titer monthy for 6 months, then bimonthy for 6 months, then yearly.
5) Biweekly chest x-ray and examination during therapy, then every 3 months during the first year of follow-up.
6) Interval follow-up of any known metastatic focus of disease.
7) Continue contraception for 1 year following remission.

A significant number of patients with either non-metastatic or good-prognosis metastatic disease fail to achieve remission on the initial drug regimen. This is usually manifested by a plateaued or rising HCG titer and it may be necessary to switch to the alternate drug regimen. It is for this reason that we prefer to begin therapy with methotrexate, particularly in patients who have had recent blood transfusions, provided renal and hepatic function are normal. This allows us to get some use out of this drug while preserving the option to change to actinomycin D should serum hepatitis develop (actinomycin D has less hepatotoxicity than methotrexate). Chemotherapy is again continued until the HCG titer has reached normal pituitary values for 3 consecutive weeks.

A small percentage of patients with non-metastatic GTN will fail to achieve remission with systemic chemotherapy. Pelvic arteriography may demonstrate a focus of disease deep in the myometrium and resistant disease is manifested by persistent elevation of HCG titer despite repetitive chemotherapy. In these patients, one can consider either arterial infusion chemotherapy[19] in a last attempt to preserve the uterus or hysterectomy during chemotherapy As a general rule, we do not feel that multiple-drug therapy with its higher toxicity is warranted unless hysterectomy has been unsuccessfully attempted. Current therapy permits essentially all patients with non-metastatic gestational trophoblastic neoplasms to be cured.

Recently, Bagshawe[20] and Goldstein[21] have published their experiences in the treatment of patients with a regimen of higher-dose methotrexate alternating with folinic acid. Results have been good with a reduction of toxic complications. We are currently utilizing this regimen in a repetitive-course fashion on carefully selected patients with non-metastatic disease and similar successful results have been obtained.

Good-Prognosis Metastatic Disease

Patients with GTN with metastasis beyond the uterus may be classified as having either good- or poor-prognosis disease. The good-prognosis patient is identified by exclusion of any of the poor-prognosis criteria mentioned earlier in this article. Patients who fall into this category of disease are treated in a fashion similar to that for patients with non-metastatic disease and, once again, essentially all of these patients are curable. In the event that a resistant focus of disease develops within the myometrium, as determined by exclusion of other foci of disease and pelvic arteriography and/or CAT scanning, hysterectomy or infusional chemotherapy may again be considered.

Hysterectomy has occasionally been advocated during the initial course of chemotherapy to reduce the total tumor burden and thereby shorten the duration of chemotherapy. It should be kept in mind, however, that a significant number of patients with metastatic disease will have no tumor in the pelvis[15, 17] and that hysterectomy is usually not necessary to achieve remission. Extreme caution should be utilized when contemplating hysterectomy if there is any evidence of extrauterine pelvic extension of tumor. We generally prefer to reserve hysterectomy for surgical indications or resistant uterine disease. Other foci of resistant disease which may develop during therapy, such as an isolated pulmonary nodule, should make one consider the use of multi-agent chemotherapy, adjuvant radiotherapy, or surgical removal.

Poor-prognosis Metastatic Disease

The findings associated with poor-prognosis metastatic disease have been previously listed. Within this group of patients, studies indicate that single-agent chemotherapy will produce less than a 30% remission rate.[4, 5] For this reason, we now suggest that these patients be initially treated with more aggressive combination chemotherapy as shown in Table 4. Cerebral and hepatic metastases are managed with either 2,000 rads whole-liver or 3,000 rads whole-brain irradiation begun simultaneously with the start of chemotherapy. Toxicity with the above multi-drug regimen is considerably higher than with single-agent therapy and extreme caution should be used when a patient has impaired renal or hepatic function. Additionally, it is recommended that physicians administering this regimen have some prior experience with it because of the potential for major toxic complications. With aggressive initial management, one should expect to achieve a remission rate of approximatley 85% - 90% in poor-prognosis patients. Again, the HCG titer is monitored weekly until normal pituitary values are obtained. It has been our policy to administer one or two additional courses of chemotherapy in these patients after a negative HCG titer has been achieved. Further follow-up is similar to that for the post-molar-evacuation patient.

Table 4
Triple-Agent Chemotherapy Protocol

1) Methotrexate, 15 mgm I.M.
   Actinomycin D, 0.5 mgm I.V.
   Chlorambucil, 8 mgm P.O.
   all of the above given daily for 5 days
2) Repeat courses with minimum interval of 12 days provided:
   (a) toxicity clearing
   (b) WBC greater than 3000/mm³, granulocyte count greater than 1500/mm³, and platelet count greater than 100,000/mm³
   (c) normal hepatic and renal function
3) Weekly HCG titer until within normal pituitary range followed by 1 or 2 additional courses of chemotherapy depending on toxicity.
4) Follow-up HCG titer monthly for 6 months, then bimonthly for 6 months, then yearly.
5) Biweekly chest x-ray and examination during therapy, then every 3 months during the first year of follow-up.
6) Interval follow-up of any known metastatic focus of disease.
7) Continue contraception for 1 year following remission.

Finally, we have had some experience with other combinations of chemotherapy for patients with disease resistant to single- and triple-agent chemotherapy. Most promising of these regimens is the Bagshawe Chemoma regimen which utilizes seven drugs during a 9-day treatment cycle. Remissions have been achieved in the first five of six patients with resistant, poor-prognosis disease treated with this protocol.[22]

Comment

Prior to the use of chemotherapy, gestational trophoblastic neoplasms carried an unusually poor prognosis. Subsequent refinements in clinical staging of patients, treatment selection, and HCG detection have permitted high survival rates to be achieved with almost any stage of disease. Despite this, there remains a population of patients in whom drug-resistant disease develops. In most of these patients, this is the result of less than adequate or non-aggressive inital therapy as well as the lack of careful post-molar-pregnancy surveillance and these patients should therefore be salvageable with better standardization of care.

Standardization of care cannot be overemphasized. Brewer,[23] in a large comparative study, showed that the mortality rate in patients treated initially at non-centralized treatment facilities was 26% as compared to a 6% mortality rate for the center-treated group. This was in spite of the fact that 30% of the initially non-center-treated patients were eventually transferred to the center. When patients with non-metastatic disease were eliminated from both groups, the mortality rate was 13% in the center-treated patients as opposed to 40% in the non-center-treated patients. This striking difference in survival has been the motivating force in the evolution of centralized treatment facilities to assist in the mangement of patients with this relatively rare disease.

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Ophthamology

Tumors of the Eyelids

Robert Rubenzik, M.D.

The eyelids may be involved with a variety of benign and malignant neoplasms. Some common benign disorders include xanthelasma (Figure 1), chalazion (Figure 2) and a variety of other solid and cystic lesions (Figures 3-5). Among malignancies, the most common is basal cell carcinoma. Less common malignancies include squamous cell carcinoma and a variety of adrenocarcinomas of the sebaceous and meibomian glands. Each of these lesions usually presents as an asymptomatic nodule on or beneath the skin of the lid. They often grow, but the growth rate varies from lesion to lesion. It is often possible to make an educated guess as to the histopathology of one of these lesions by its appearance. For example, the basal cell carcinoma usually resembles a crater with a raised "pearly" margin. But variations exist (Figure 6), and the educated guess is often just that. No one can consistently predict the nature of a lid lesion without biopsy.

From: 3201 West Peoria, Ste D-802, Phoenix, AZ 85029

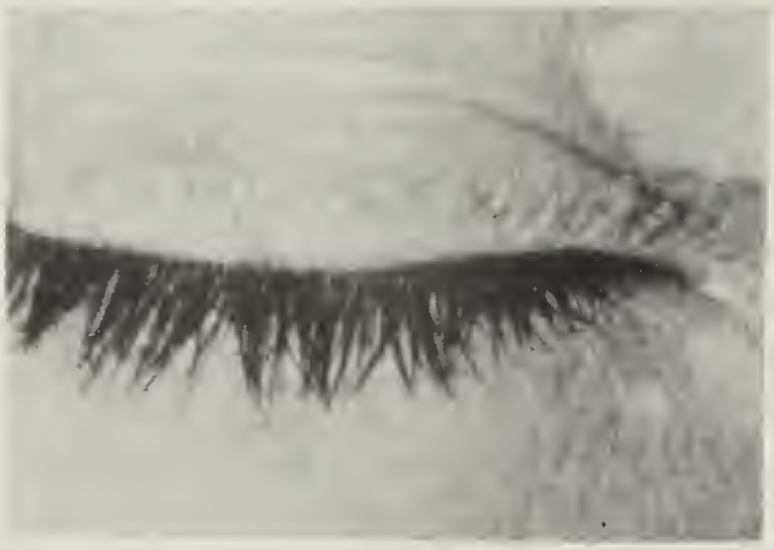

Figure 1
The typical appearance and location of a xanthelasma.

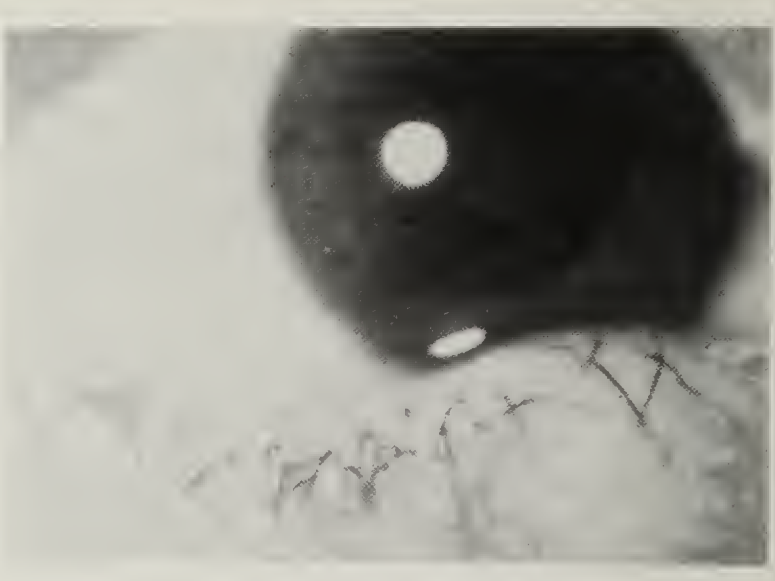

Figure 2
A typical chalazion (lipo-granuloma).

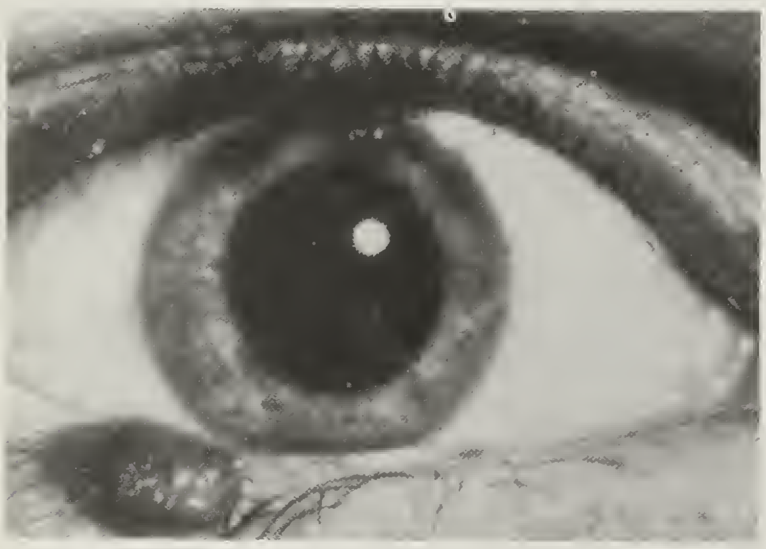

Figure 5
A nevus of the lid margin.

When a lid lesion is to be biopsied, a choice must be made: whether to do an "excisional" (presumably total) biopsy or to "shave" the lesion level with the surrounding tissue with the idea of obtaining a piece for histologic examination. Most of the time an excisional biopsy is not needed, since we are interested in knowing only whether the lesion is benign or malignant. If it is benign, no further treatment may be indicated. If it is malignant, plans may be made for further excision. The "shave" biopsy technique is an office procedure and does not require sutures.

When the lesion is found to be benign, occasional follow-up is all that is needed with the following exceptions: Some inflammatory lesions such as the chalazion or pyogenic granuloma may be stubbornly recurrent. Injection of these lesions with steroid usually will cause them to regress without further treatment. In addition, an occasional benign appearing lesion is in a

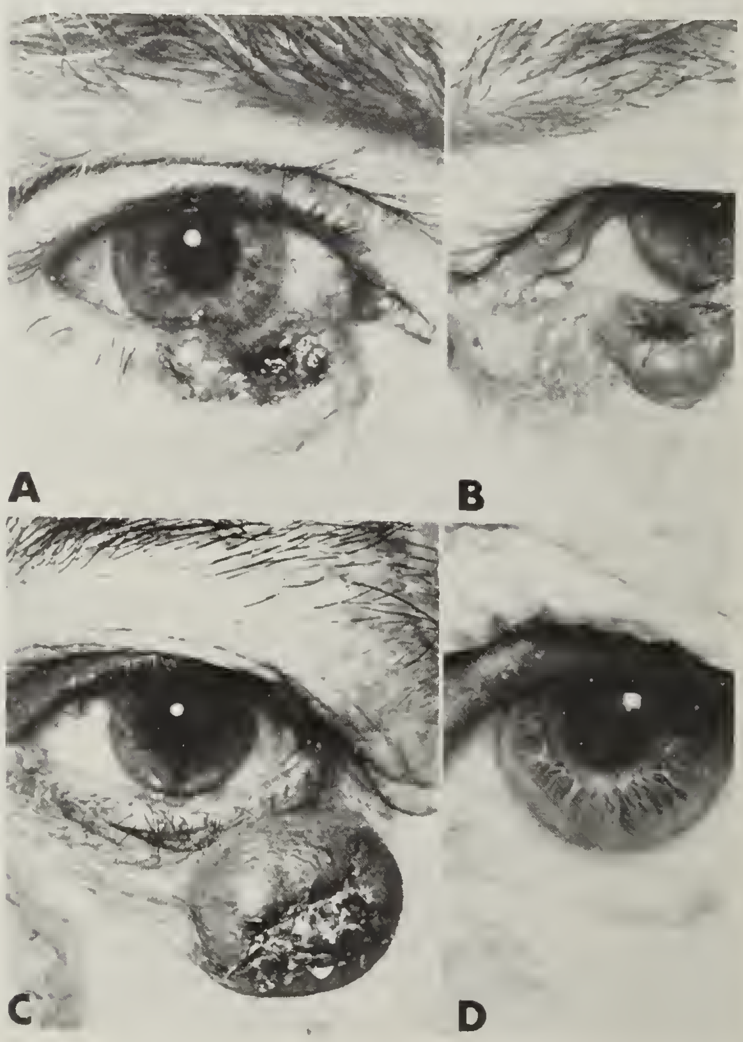

Figure 6
Biopsy - proven basal cell carcinomas of the lower eyelid. Note the great variation in appearance.

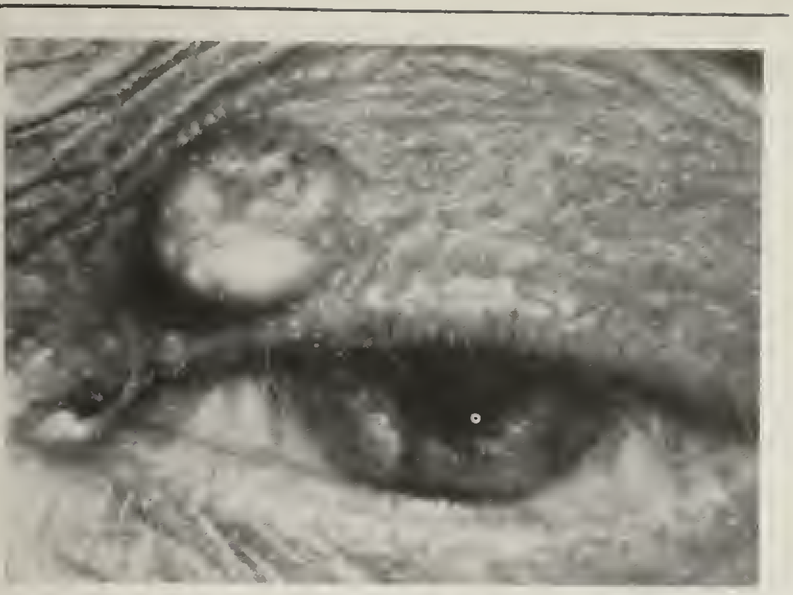

Figure 3
A sebaceous cyst of the upper lid.

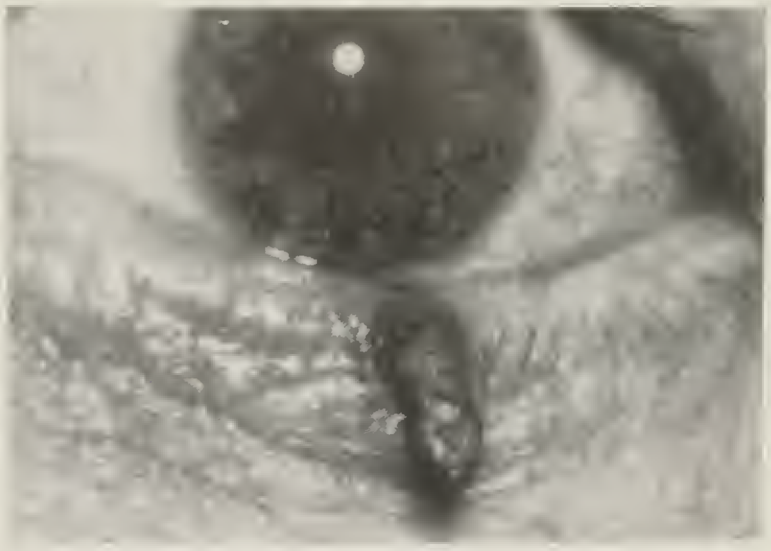

Figure 4
A cutaneous horn. This is a variant of senile keratosis.

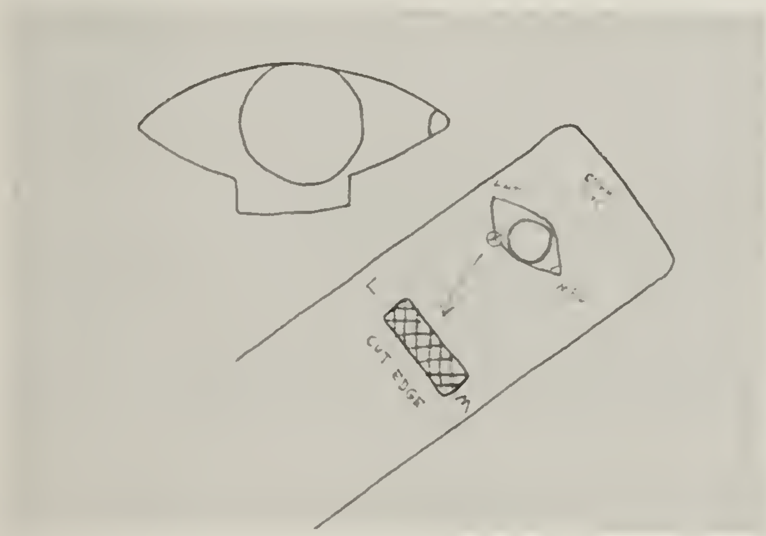

Figure 7
When a lesion is sent to pathology from the operating room for frozen section it should be oriented on a clearly-labled surface, such as a tongue blade, for the benefit of the pathologist. With this technique the pathologist may examine the cut edges for residual tumor.

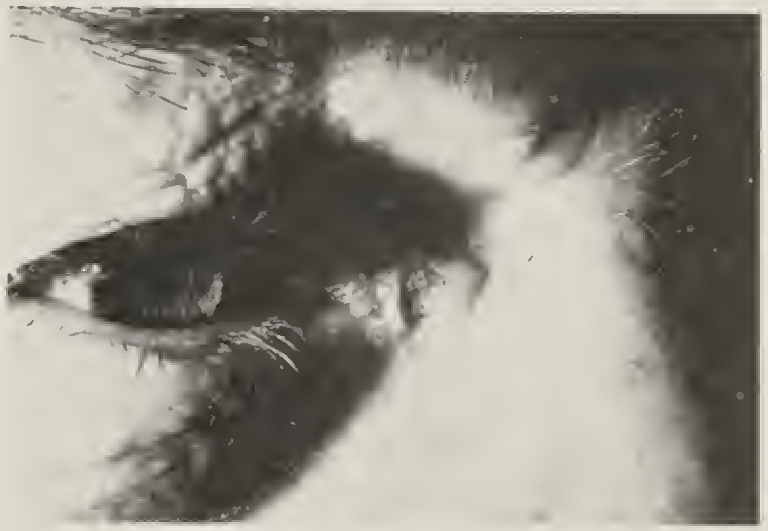

Figure 8
A basal cell carcinoma in the region of the medial canthus. though the recurrence rate following incomplete excision (such as biopsy) is only 20-30%, a recurrence in this region may prove fatal. For this reason, total excision with frozen section control is advised.

position that does not lend itself to "shave" biopsy. If a lesion does not project above the surface of the surrounding tissue any biopsy will leave a disfiguring defect. In such cases and excisional biopsy should be done, as the cosmetic results following repair are generally good.

Management of malignancies requires some planning. Even when the histopathology of the lesion is known, its extent is not. The most prudent technique at the moment seems to be complete excision under frozen section control followed by reconstruction of the resulting defect (Figure 7).

What if after excision and reconstruction it is discovered on permanent sections that a malignant lesion was incompletely excised? This depends on the type of tumor and its location. For example, squamous cell carcinomas has metastatic potential and should be re-excised, again with frozen section control of the wound margins. The recurrence rate if this lesion is inadequately treated is high. The same applies to adenocarcinoma of the sebaceous or meibomian glands.

If excision of a basal cell carcinoma has been done without frozen section control, retrospective studies reveal the incidence of inadequate excision (judged on permanent section) to be on the order of 30%. Other studies on this subject show the overall recurrence rate to be only 10%. For unknown reasons, the likelihood of tumor recurrence in a give inadequately-excised basal cell carcinoma is on the order of only 2 - 30%. In addition to this low recurrence rate, the recurrence tends to be local and not metastatic. The concensus among oculoplastic surgeons as regards the inadequately-excised basal cell carcinoma is this: most of the surgical sites may be safely watched for evidence of tumor

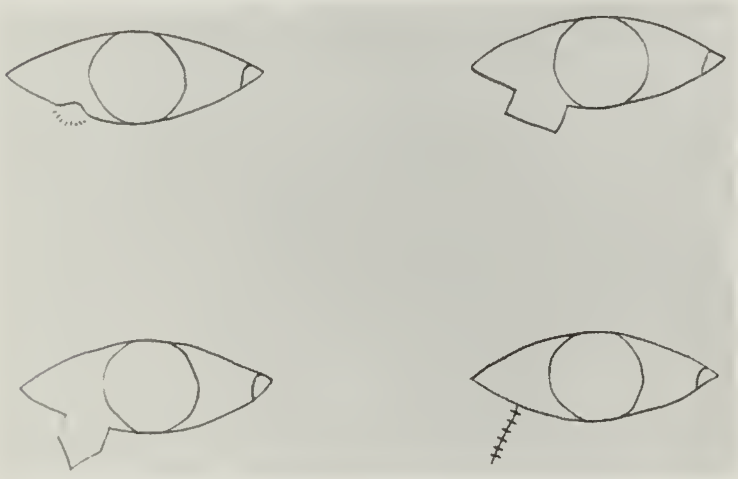

Figure 9
The basic technique of surgical removal of a lid lesion. Upper left: the preoperative location of the tumor. Upper right: complete excision is carried out. Frozen section of the three cut edges confirms complete removal. Lower left: the defect is converted to the shape of a pentagon to facilitate closure. Lower right: direct closure of the wound with interrupted sutures.

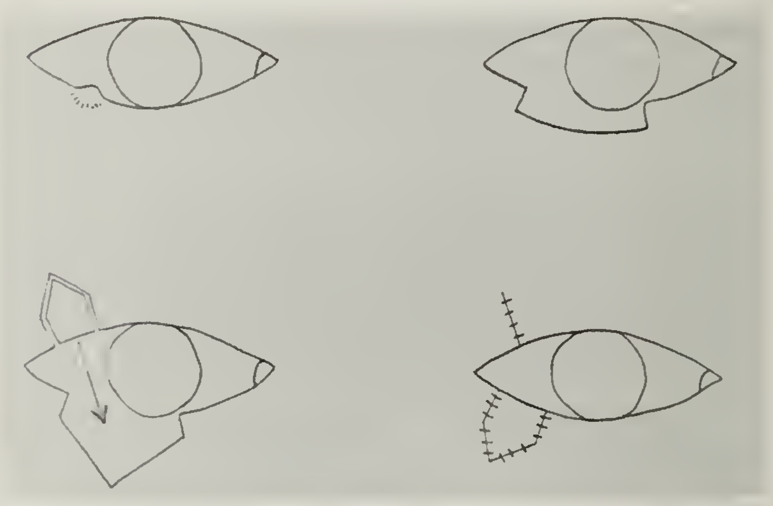

Figure 10
When the wound following tumor excision is too large to permit primary closure, the defect may be closed with a free graft from another lid. Upper left: the lesion before removal. Upper right: removal of the tumor, leaving a large defect in the lid margin. Lower left: removal of a pentagonal full-thickness graft from the upper lid. This may be on the order of 1/4 of the upper lid margin. Lower right: the upper lid wound is closed primarily. The graft is sutured into place in the lower lid.

recurrences. Reoperation is necessary only if a new tumor appears. The treatment of recurrences is, once again, complete excision under frozen section control. In most areas recurrences are amenable to futher treatment if they are spotted promptly. In the region of the inner canthus, however, a recurrence may quickly involve the paranasal sinuses and orbit before it is detected. Inadequately-excised basal cell carcinomas of the inner canthus should be re-excised, as though one were dealing with a more malignant tumor. (Figure 8).

Reconstructive techniques are varied, ranging from the ridiculous to the sublime. It is unwise for the surgeon to commit himself preoperatively to a specific reconstructive technique. It is probably better to do a good excision and then assess the availability of remaining eyelid tissue for closure of the wound. This availability factor is related to the patient's age, since young people tend to have tighter lids. Closure of a defect amounting to over 1/4 of an eyelid may pose technical difficulties. In an elderly person with lax eyelids, a defect of half the lid may often be closed primarily. The most reliable technique, the easiest, and the most likely to produce a good cosmetic result is usually the simplest, i.e., connecting the two cut edges together with fine sutures (Figure 9).

My general rule of thumb is that when the lid defect is on the order of 1/4 of the eyelid, direct closure should be attempted. A defect of 1/3 of the lid may usually be closed by severing the lateral canthal tendon followed by direct closure of the wound. In large defects, a favorite technique is to repair the defect with a free full-thickness graft from another eyelid (Figure 10). In the event that the entire lid must be sacrificed, the opposing ipsilateral lid may be used to create a new eyelid.

Pediatrics

A Perspective on Child Abuse

Warren F. Gorman, M.D., F.A.C.P.

Definitions

Child abuse is a medico-legal term for the battering or traumatizing of children. Other terms for child abuse include non-accidental injury, extreme neglect, sexual abuse, severe malnourishment, non-accidental burns and the exposure of children to toxic substances. Under many statutes a "child" is a person under 18, but some set this age as low as 12.[1]

In November of 1961 Dr. C.H. Kempe noted on his pediatric service in Denver, four infants suffering from the "parent-inflicted battered-child syndrome." Three died. His University of Colorado group surveyed 71 hospitals, finding 302 battered child cases in one year, of which 32 died and 85 suffered permanent brain injury. Contacting 77 district attorneys, they reported 447 cases in one year, with 45 deaths and 29 permanently brain damaged. In their definitive 1962 publication, Kempe's team noted that when the patients were under the age of three, the trauma was repeated and that the time between injury and examination was excessive.

Subsequent studies independently confirmed these findings and also showed that contusions are the most common trauma of child abuse, but that head and brain injury is second in frequency.[5] [6] Head injuries include skull fracture; brain trauma including subdural hematoma, brain injury with or without post-traumatic seizures, and whiplash injury of the brain[7] from shaking the infant without direct trauma to the head,[8] the latter showing no external mark of injury. Leg fractures are more common than those of the upper extremity, but teaching hospitals have x-ray films of an infant's fingers flattened by a hammer. Teenage alcoholism and drug abuse suggests chemical child abuse, and an observer indicates that affirmative encouragement of sloth and gluttony in children is child abuse, since they lead to heart attacks in adult life.

Despite mandatory reporting and a central registry, child abuse is under-reported. In June of 1978, President Carter said, "One million children in our country were abused last year by parents and others." In November of 1978 a group commissioned by the National Institute of Mental Health reported a national total of two million, noting that 4% of children under 17 were abused.[10] The most frequent victim is not the first child of a family unit, and is not the only child. Neglect and maltreatment, including statutory sexual abuse, is twice as frequent as child battering.[11] [12]

In a normal child-parent relationship, "claiming" develops[13] in which the new infant first is amalgamated with the mother's relationships. The mother (or both parents) then identify with the baby and generate positive feedback. (This is associated with partents's normal over-evaluation of the infant.) But if this positive feedback fails, Morris suggests there can be a *psychological miscarriage,* in which the feedback becomes negative. In this latter setting, if the parent is stressed, he or she can perceive the child as an attacker and the adult as the victim, then attack the child in an attempt to relieve their adult stress. "Claiming," plus two years of what Winnicott calls, "Ordinary good mothering"[14] is generally adeuqate to prevent later child abuse.[13]

Milowe noted children who were attacked in sequential foster homes, where no other child was ever battered. Did these children[13] actively provoke the battery? Is there a congential or organic cause of this child's behavior? We know of temporal lobe and limbic system disorders with assaultiveness as a clinical feature.

Many parents of abused children have themselves been abused in their childhood. A personality profile of the abusing parent shows such parents making excessive, lofty demands of the child. When the child fails to meet these standards, they attack. Mothers who abuse children often have given up hope of ever finding a mother ideal. They also "have a heavy sense of aloneness and worthlessness and a morbid desire for the child to provide their unheeded needs of yesterday." When the child fails to heed, he or she is beaten.[13]

Repetition compulsion, as it is seen in obsessive patients, is frequently noted and the excessive cleanliness of compulsive patients is noted in home of child abusers, even where the child has been abused by neglect.[13] Of these neglected children, Redl[15] writes "The children who hate. . .are the children of neglect. They have been chronically traumatised, through repeated frustrations of many of their basic needs. (Indeed) we might speculate that they suffer from a disease entity directly stemming from neglect itself, which might be called 'neglect edema.' Their frustrations swells and festers until even their frustration, which is minor and painless in terms of the normal, becomes for them an intolerable challenge to

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From: 5602 E. Nauni Valley Dr., Scottsdale, AZ 85253

control what they cannot meet. For each frustration, no matter how small the issue may be, is lumped together with the frustrations out of the past."

Psychosis, or a severe disorder of appreciating and adapting to reality, is reported in about 10% of child abusers.[6] [16]

Others assert that the reversal of child-parent roles is a disturbance of reality testing; that under stress, child abusers develop an episodic psychosis, in which they attack the child under the delusion that they, the adults, are protecting themselves from being destroyed.[13]

Treatment is performed primarily with the adults, and seldom solely with the children; it is usually group psychotherapy. Children are usually kept in the formerly abusing home during treatment, but for emergencies, some states provide emergency foster homes or even emergency foster parents in the child's abandoned home. Results for those who attend treatment sessions are good.[16] [17]

To date, the best prevention of child abuse consists of family education for family planning.[1] Keeping in mind that the surviving abused child, on becoming fertile, may abuse his or her children, we expect benefit from the California statute against child abuse, which provides for parent education and training services to prospective parents.[18] Arizona statutes provide a misdemeanor penalty for a person who "permits the life of such a minor to be endangered, its health to be injured, or its moral welfare to be imperiled. . ." A full report of child abuse must be made to a municipal or county peace officer or the Department of Economic Security, Division of Protective Services, (Telephone **269-1401**).

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Psychiatric Disorders

Human Nature: The Personality Types

William B. McGrath, M.D.

Excluding some of the major psychoses and organic brain syndromes, primary diagnosis in psychiatry is not diagnosis at all. It is no more than a repeating or rewording of the chief complaint. Documentation of the most distressing symptom as a diagnosis contributes little or nothing to our understanding of a patient.

"I am depressed" becomes Depression.
"I am nervous" is classified Anxiety Reaction.
"I have headaches" is translated Cephalgia
"My son is rebellious" equals Unsocialized Aggressive Reaction of Adolescence.

Nor is very helpful information conveyed by terms like "Masked Depression;" i.e., one which manifests itself in psychosomatic illness or alcoholism or the "acting out" disorders of childhood and adolescence. (Incidentally, one does not usually make a personality diagnosis in preadult years).

The appalling shallowness and circularity of primary diagnoses betrays our ignorance of etiology. From such superficial labels as depression or anxiety, etc., we can derive no guidance in treatment planning or with regard to the attitudes of therapists and family; nor can we even speculate about prognosis, suicide risk or the prevention of future attacks.

This is one of the reasons why psychiatrists sometimes seem interchangable with psychologists, sociologists, clergymen, social workers and a variety of self-anointed counsellors: "humanistic," marital, vocational, nutritional, etc.

What's wrong? In the teaching of psychiatry to non-psychiatric professionals and in the education of the public, the ominous significance of the personality disorders has been overlooked or neglected. Our official "Diagnostic and Statistical Manual of Mental Disorders" and most textbooks fail to point out that *almost every neurosis or psychosomatic illness is a complication of one or another of the classifiable personality disorders.*

From: Camelback Hospital, 5055 N. 34th Street, Phoenix, AZ 85018. Dr. McGrath, Medical Director.

Normal persons are not very vulnerable to "functional" disorders. In adapting to changing conditions they can choose wisely from a full and varied repertoir of reaction patterns and traits. In contrast the patient with a personality disorder is arrested or fixated at some immature, circumscribed and repetitious way of coping with situations, unsuccessfully.

Anyone who wants to organize and enrich his understanding of human nature must first become thoroughly familiar with each of the eight or so different personality types. They are constellations of traits which were more or less imposed on the child or which seemed to him to have survival value. They are no longer necessary or appropriate in adult life, though the individual is afraid to relinquish them or is surprisingly unaware of the need for change.*

Noting two or three fairly constant or cardinal traits, we can anticipate the others which will fill out a particular constellation. When one observes habitual punctuality and meticulousness, he will look for the stubbornness and miserliness of the obsessive-compulsive personality. Or, one who really knowns the meanings of histrionic will not be dismayed at the theatrically stormy and very self-centered moods and behavior of that type of patient.

The predictive value of accurate appraisal at this fundamental level becomes obvious. And recognition of the personality type affords clues to the patient's background and channelizes and expedites our questioning.

Among the prevailing tautological primary diagnoses (depression, alcoholism, anxiety, colitis) depression is the commonest. Using it as an example, and given some precipitating event, we might ask: Why does this individual's mood disorder seem more than normally severe and prolonged? Even the briefest hint of an answer might illustrate an enlightening value when differential diagnosis is based on the personality type.

Pre-Psychotic Personality Pattern Disorders:

1. Inadequate: The traumatic event has proven again that he never learned to take adult responsibility. Unable to keep his own resolutions he is over and over again the tearful victim of circumstances.

2. Schizoid: Something has reinforced his conviction that he will never understand others or himself be understood; he can never experience the joy of loving and being beloved. This is unspeakably sad for him and for those who try to keep him warm.

3. Cyclothymic: An unfortunate event will just confirm the melancholy pessimism of this constitutionally depressive. Or the opposite: The perennial optimism of the hypomanic may have been punctured by the sharp spikes of reality.

4. Paranoid: All his vigilance and all his struggles for groundless self-importance have brought him only scorn and indifference and rejection.

Pre-Neurotic Trait Disorders.

5. Obsessive-Compulsive: His is the classical and repetitive syndrome, IDD idealism, disillusionment, demoralizaiton. The perfectionist simply cannot attain perfection nor impose it on those around him.

6. Passive-Aggressive: the passive one's negativism will no longer arouse everyone's apologetic guilt, nor will people continue coaxing him to relinquish his sullen depression. The agressive will push away gentler friends (and customers) and finally be felled by overpowering fate.

7. Histrionic: People will come to realize that he or she is always on stage and never quite sincere, and they will begin to ignore the dramatic seeking of attention.

8. Sociopathic: Sometime inevitably he will have to suffer the painful consequences of his disregard for the rights of others and his own lack of self-respect.

The primary or admitting diagnosis (depression, anxiety, etc.) might in every instance be the same. But each case's clinical course will be entirely different from all the others!

Without fundamental knowledge of the personality disorders, a therapist of whatever kind or degree will be insecure and ineffectual, forever an amateur. Benevolence, compassion and persuasiveness are worthless without this deeper insight. Similarly, one who treats only the chief complaint is missing the most mutually rewarding work of psychiatry.

The terms we use—schizoid, paranoid, histrionic—seem judgemental, almost derogatory. On the contrary, fuller understanding brings greater acceptance. When you have traced the sources of a particular personality pattern or trait, both you and the patient will ask yourselves, "How else could we expect him to be?" With this kind of understanding and with you at his side the patient can begin bypassing his morbid repetition compulsions, experimenting with new and more mature ways of viewing himself and adapting to the situations in which he (literally) finds himself.

Working knowledge of the personality types is not easy to acquire. (Thank goodness; because any snap judgement is an insufferable conceit!) Nevertheless one can think about friends and acquaintances, observing their habitual ways of coping; aggressive or passive-aggressive, perfectionist or histrionic, optimist or pessimist. They stay "in character."

With thorough knowlege of developmental psychology, history taking becomes an art. Categorical personality diagnosis, however, still awaits careful study of a patient. Especially needed are the impressions and experiences of others (family members, nurses' notes) who encounter the individual in other settings than the doctor's office.

The personality disorders have in common such maladjustments as are rooted in one or another kind of persistent immaturity. Hence among the types some

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*"Of To be a Judge of Character, Part I," Vol. 24, No. 7, p 630, 1967.
"Of To be a Judge of Character, Part II," Vol. 24, No. 11, p 1095, 1967.
"Hysteria", Vol. 33, No. 4, p 309, 1976.
"Paranoid Personality," Vol 35, No. 9, p 604, 1978.

overlapping is to be expected. When it proves difficult to classify a given case, one thinks first of one's undeveloped perceptiveness. Or more probably one is dealing with a reasonably normal and mature person. Such a person can engage (ad hoc) whichever pattern or trait seems suitable to the occasion.

Whatever the immediate problem or primary diagnosis; whatever the spiritually stunting or twisting conditions of formative years (as the twig is bent), we have to accept the patient as he is. He can never step back to get a three dimensional view of himself. Ahead of him, as we light his way, are emancipation from the slavery of the past and such self-determination as can be achieved only in adult life.

In general medicine and in the other specialties a patient's life might sometimes be at stake. At stake in the diagnosis and treatment of personality disorders is the *value* of the patient's life; not just now but as it impinges on those around him.

Radiology

Case of the Month No. 38

Anna R. Nussbaum, M.D.
John c. Bjelland, M.D.

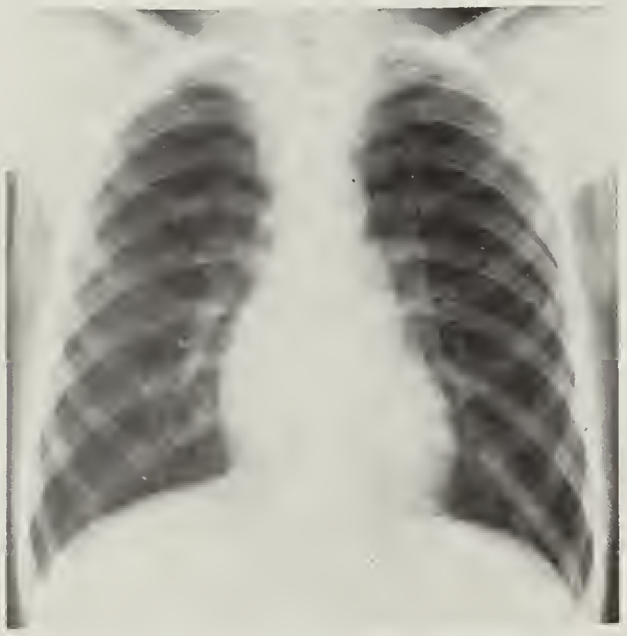

Figure 1

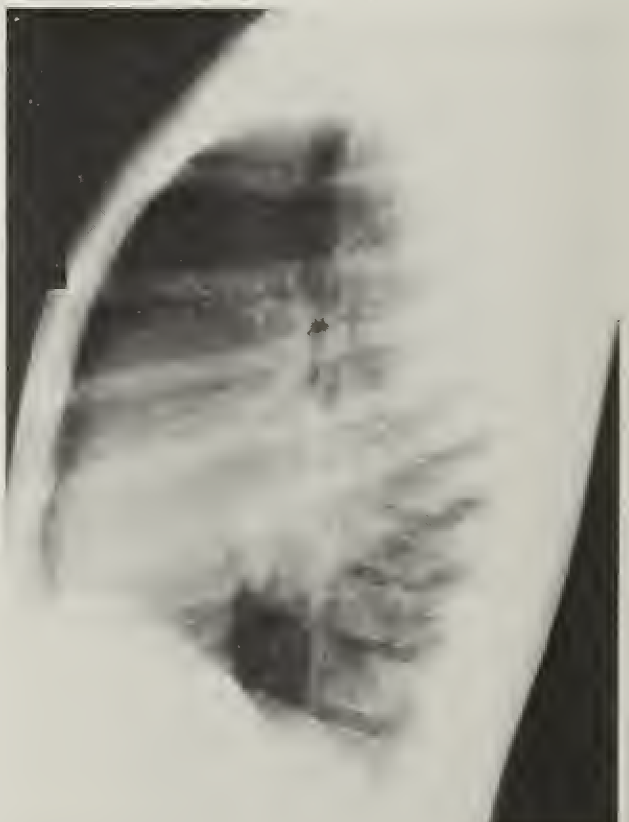

Figure 2

A previously healthy eight-year old male developed an acute febrile illness, with the major symptoms being rhinorrhea and a "hacking," non-productive cough. He was medically evaluated and a basline chest radiograph was obtained to rule out the possibility of pneumonitis (Figures I and II). What is the most likely diagnosis?

From: University of Arizona Health Sciences Center, Dept. of Radiology, Tucson, AZ 84724.

Continued on Page 466

State of the Art

Aminoglycoside Antibiotics

Stanton G. Axline, M.D.
John N. Galgiani, M.D.

Eric H. Prosnitz, M.D., Editor

Historical Aspects

The aminoglycosides constitute an economically important and clinically useful group of antibiotics that were preceded in availability only the by penicillins. Streptomycin, the first of this class of drugs to be discovered, was introduced into clinical medicine in 1944. This was followed five years later by neomycin. During the following twenty years only two aminoglycosides were introduced, kanamycin in 1958, and gentamicin in 1969. During the past decade research into the aminoglycosides has been intensified, resulting in the introduction in 1976 of both tobramycin and amikacin. Two additional aminoglycosides, sisomycin and netilmicin, are in advanced stages of clinical trials as investigational drugs. In addition, several other aminoglycosides have been discovered but are not included in this review since they have not received widespread use in clinical medicine.

General advances in antimicrobial availability, as well as introduction of new aminoglycosides, have resulted in drastic shifts in our use of drugs of this class during the past ten years. Kanamycin, for nearly a decade the most widely used aminoglycoside, has now been largely replaced by gentamicin.[1] Tobramycin is perhaps the second most widely used aminoglycoside, followed by amikacin. At the present time streptomycin is limited almost exclusively to treatment of tuberculosis, and neomycin for parenteral use is of historical interest only.

Pharmacology. Aminoglycosides are bacteriocidal antibiotics and the mechanism of action of all drugs of this class are indentical. They act by binding irreversibly to a specific protein receptor site on the 30S ribosomal subunit which blocks the "recognition step" and induces misreadings of the messenger RNA delivered to the bacterial ribosome, thus interfering with protein synthesis.[2]

Since aminoglycosides are rather basic compounds, are very poorly absorbed when administered orally unless there is disruption of the integrity of the intestinal tract. Thus, to be effective systemically, aminoglycosides must be administered parenterally. Any of the aminoglycosides can be adminstered by either the intravenous or intramuscular routes. Their volume of distribution is the extracellular fluid compartment and thus is approximatley 25% of lean body weight in adults and greater in children. None of

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From: Univ. of Arizona Health Sciences Center, Tucson, AZ 85724. Veterans Administration Medical Center, Tucson, AZ 85723. Dr. Stanton G. Axline, Assoc. Prof. of Internal Medicine and Chief, Infectious Disease Section, Univ of Arizona Health Sciences Center, and Assoc. Chief of Staff for Research, Tucson Veterans Administration Medical Center. Dr. John N. Galgiani, Assist. Professor of Internal Medicine, Infectious Disease Section, Univ. of Arizona Health Sciences and Chief, Infectious Disease Sect., Tucson Veterans Administration Medical Center.

the aminoglycosides penetrate well into the uninflamed meninges, and there is variable penetration in the presence of inflammation.[3] The aminoglycosides are excreted almost exclusively by the kidney by glomerular filtration. Thus, the half-life of the drug in its volume of distribution is determined largely by renal clearance. Although there is considerable overlap in the half-lives of the various aminoglycosides, it may be useful to divide them into two groups. The first group consists of streptomycin, kanamycin, and amikacin, which have half-lives of approximately three to four hours. As a result they are frequently administered at intervals of twelve hours to patients with normal renal function. The second group of aminoglycosides, consisting of gentamicin and tobramycin, have half-lives of two to three hours. As a result they are administered at intervals of approximately eight hours to patients with normal renal function.[4, 5]

Spectrum of Activity

The aminoglycosides exhibit marked differences in their spectum of activity. With the introduction of streptomycin, effective drug therapy was available for the first time against tuberculosis, with a resulting reduction in mortality of miliary tuberculosis from 100% to 47%. All of the aminoglycosides have antituberculous activity, roughly in the following order of potency: amikacin> kanamycin> streptomycin> gentamicin. Despite the fact that amikacin and kanamycin appear more active *in vitro*, streptomycin has had extensive clinical use and remains the aminoglycoside most often used in the treatment of tuberculosis.

Streptomycin was found to be effective against the Enterobacteriaceae, but not against *Pseudomonas aeruginosa* or other pseudomonas species. However, the utility of streptomycin for treatment of such gram-negative infections has always been limited by the observation that sensitive organisms both *in vivo* and *in vitro* rapidly developed resistance. This can occur within 48 hours after initiating therapy.

Neomycin exhibited a spectrum of activity similar to that of streptomycin but was considerably more potent. Further, resistance did not develop as rapidly *in vitro*. Neomycin, an extremely useful antibiotic for parenteral use, was discarded as kanamycin became available. Kanamycin exhibits the same spectrum of activity as streptomycin against Enterobacteriaceae and, in addition, is effective against a number of indole-positive and indole-negative proteus strains. It has no activity against *Pseudomonas aeruginosa*. Although it exhibits substantial antistaphylococcal activity, it has not bee used widely for this purpose since the availability of penicillinase-resistant penicillins.

With the introduction of gentamicin the spectrum of aminoglycoside activity has been broadened to include *Pseudomonas aeruginosa*. In addition, it is generally effective against a higher precentage of the Enterobacteriaceae than kanamycin, neomycin or streptomycin. In a recent nationwide survey 97% of *Citrobacter* species, 97% of *Enterobacter* species, 99% of *Escherichia coli*, 97% of *Klebsiella pneumoniae*, 98% of *Proteus mirabilis*, and 92% of *Pseudomonas* species were sensitive to gentamicin.[6] Of the gram-negative rods, only *Alcaligenes* species, *Proteus rettgeri*, *Providencia*, and *Serratia* species are not predictably sensitive to gentamicin.

Tobramycin has a spectrum of activity nearly identical to that of gentamicin. However, approximately one-third of *Pseudomonas aeruginosa* strains that are resistant to gentamicin may be expected to be sensitive to tobramycin. Amikacin exhibits the spectrum of activity common to tobramycin. It also includes many strains of pseudomonas documented to be resistant to gentamicin and tobramycin. All the aminoglycosides uniformly lack efficacy against streptococci, meningococci, pneumococci, and all anaerobic bacteria, including streptococci, clostridia, and bacteroides species.

Clinical Conditions requiring Aminoglycosides

The principal indication for aminoglycoside use is serious gram-negative aerobic bacterial infections, usually due to organisms resistant to less toxic antimicrobials such as ampicillin or the cephalosporins. This frequently includes initial therapy in suspected gram-negative sepsis in which the bacterial agent has not yet been identified or its antimicrobial susceptibilities are not yet known. In such cases, when additional culture results become available a less toxic effective agent often can be substituted, thus limiting the aminoglycoside usage to the first few days of therapy. Because gram-negative aerobic bacteria may represent only a part of polymicrobial infections, it may be necessary to use one or more additional antimicrobial agents concurrently.

The selection of the aminoglycoside should take into consideration several factors, including the route of administration, the likely site of infection, the infecting agent, and its probable antimicrobial susceptibilities. If specific susceptibility data are not available, knowledge of the resistance patterns seen previously in the same locale or hospital can provide guidelines. Generally, it is advisable to use an antimicrobial agent with as narrow a spectrum as possible. Kanamycin would be suitably active for many infections requiring aminoglycosides and has the narrowest spectrum of activity as compared to gentamicin, tobramycin and amikacin. Since the recommended route of administration is intramuscular, kanamycin often is used to treat infections in infants where this route is more convenient than intravenous administration. It is less commonly used in adults where intramuscular injections in debilitated persons are often a problem. In areas where gentamicin resistance is not a common problem, it remains the aminoglycoside most comonly used in adults. We have reserved amikacin use for infections due to gentamicin-resistant bacteria, still uncommon at our institution.

The use of aminoglycosides that show *in vitro* activity against staphylococci warrants particular attention. It should be borne in mind that only one study has been published that attempted therapy of diseases due to coagulase positive staphylococci with gentamicin alone.[7] This report raises serious questions concerning the efficacy of this agent alone in treating such infections. Since other less toxic agents are available for treatment of documented staphylococcal disease it would seem prudent not to use aminoglycosides alone.

Certain infections other than those due to staphylococci may fail to respond despite demonstrated sensitivity of the bacteria *in vitro*. Although aminoglycosides diffuse into most tissues well, penetration into the cerebrospinal fluid is variable and intravenous therapy alone cannot be used reliably to treat gram-negative menignitis in adults. For such infections intrathecal administration is usually necessary to assure adequate CSF concentrations.[8] In other situations local environmental factors at the site of infection may inhibit the effect of aminoglycosides. For example, urine may sometimes severely impede the action of gentamicin because of its acidity and high osmolality.[9] Although aminoglycosides are often effective in the treatment of urinary tract infections this inhibitory effect may be important when urinary concentrations of the antimicrobial agent are decreased either by reduction in dosage or because of decreased excretion due to renal insufficiency. Lowered pH in purulent synovial fluid may also be a factor in the slow response of septic arthritis treated with aminoglycosides, underscoring the need for adequate drainage of infected joints in addition to antimicrobial therapy.[10] Finally, one of the most difficult settings in which to eradicate infection is that of the immunocompromised neutropenic host. Experimental evidence raises doubts about the adequacy of aminoglycoside therapy alone in treatment of serious gram-negative infections.[11] In this setting at least two antimicrobial agents should be used routinely with their selection allowing overlapping coverage. Once a specific causative microorganism has been indentified, therapy should be modified to include two agents, both of which are active against the infecting agent. As discussed below, such combinations may be more than additive in their effect.

Synergism

Enterococcus. A particularly important clinical property of the aminoglycosides is that in addition to being effective individually, they frequently act synergistically with other antimicrobial agents against a number of bacteria. The first described, most thoroughly studied of the synergistic reactions, is that of the aminoglycosides and penicillins against the enterococcus. The enterococcus, only partially inhibited by penicillin and always resistant to clinically achievable levels of streptomycin, is killed by a combination of the two drugs. The mechansism of the synergistic action is now quite clear. Aminoglycosides penetrate the bacterial cell wall relatively poorly. However, when a cell wall-active antimicrobial such as penicillin is used concomitantly the resultant injury permits streptomycin to penetrate more easily to reach the bacterial ribosomes.[12] Only when the enterococcus contains aminoglycoside-resistant ribosomes - i.e., when the minimal inhibitory concentration cannot be achieved even with thousands of micrograms per milliliter of drug - does this combination become ineffective. Of the aminoglycosides currently available, gentamicin is the most predictably effective with regard to its synergistic activity against the enterococci. Although penicillin and streptomycin were originally used for their synergistic activity against the enterococcus, with the development of newer agents it now appears that ampicillin and gentamicin is the most effective combination. This stems from the finding that a higher percentage of enterococci will have gentamicin-sensitive, rather than streptomycin-sensitive, ribosomes. In addition, the activity of ampicillin against the enterococcus is greater than that of penicillin G.

Staphylococcus. Although gentamicin, tobramycin, kanamycin, and amikacin are active *in vitro* against more than 90% of the coagulase positive staphylococcal isolates, the use of aminoglycosides alone for staphylococcal infections is not accepted as good clinical practice. Serious staphylococcal infections, particularly endocarditis, are difficult therapeutic challenges. Even with the best available single antistaphylococcal drugs failure and relapse are not infrequent events. Striking synergism between aminoglycosides and the penicillinase-resistant penicillins have been demonstrated *in vitro*. Further, such combinations have resulted in more rapid resolution of endocarditis in experimental models. Thus, combination therapy may have merit for treatment of patients with serious staphylococcal disease, including endocarditis.

Pseudomonas. Gentamicin, tobramycin, and amikacin exhibit *in vitro* effectiveness against *Pseudomonas aeruginosa* and other pseudomonas species. Despite the *in vitro* sensitivity, clinical observations have shown that patients, especially those who are granulocytopenic with infections due to *Pseudomonas aeruginosa*, have a poor prognosis when treated with aminoglycosides alone. In searching for potential solutions to this problem it was observed that gentamicin exhibited synergy with carbenicillin *in vitro* against pseudomonas organisms. As newer aminoglycosides have become available it is now clear that the same general observation applies to tobramycin and amikacin as well as gentamicin. Further, ticarcillin can be substituted for carbenicillin with nearly indential *in vitro* results. On the basis of these observations it is now common practice to use an aminoglycoside and carbenicillin or ticarcillin in combination for treatment of serious pseudomonas disease, particularly in the granulocytopenic patient.

Klebsiella. More than 95% of *Klebsiella pneumoniae* organisms can be expected to be sensitive *in vitro* to the cephalosporins. In addition, these organisms are also quite sensitive to aminoglycosides. However, *in vitro* studies have demonstrated convincingly that the combination of an aminoglycoside plus a cephalosporin is often synergistic against klebsiella. Because of the high intrinsic activity of the cephalosporins against klebsiella, combination therapy is often not used. However, in serious infections a combination of an aminoglycoside and a cephalosporin may prove to be beneficial, whereas with less serious infections such as infections of the urinary tract, either a cephalosporin or an aminoglycoside alone may be satisfactory therapy.

Susceptibility Testing

Numerous variables affect susceptibility test results obtained with aminoglycosides. Bacterial inoculum size is one of the more important factors affecting the results from both broth dilutional and disk diffusion methods.[13] In addition, several studies have demonstrated that the concentration of divalent cations such as Ca++, Mg++, Zn++, and Cu++ significantly influence susceptibility results.[14] If reproducible results are to be obtained it is imperative that strictly standardized methods be employed.

Toxicity

Renal and eighth cranial nerve toxicities, shared by all aminoglycosides, constitute the major limitations to therapy with these drugs. They are both partially dose-dependent effects and can be minimized by careful attention to serum concentrations.

Drug-related ototoxicity affects both the cochlea and vestibular apparatus with corresponding damage seen in the hair cells of the cochlear duct and in the spiral Organ of Corti. The predominant eighth nerve effect of amikacin and tobramycin is on the former and of gentamicin is on the latter. The incidence of ototoxicity is one to three percent in large series. However, rates several times higher have been found in prospective studies in which pretreatment auditory measurements have been taken.[15] Ototoxicity is usually irreversible, but awareness of the complication and early detection may limit significant impairment if the aminoglycoside can be discontinued.

The risk of ototoxicity is highest in persons with an initial abnormal audiogram, ear infection, severe illness, concurrent use of another antimicrobial agent or diuretics, pre-existing renal insufficiency or high aminoglycoside serum concentrations. Recognition of these factors and particular attention by the physician to the importance of serum concentrations is essential when using aminoglycosides.

Nephrotxicity is manifested by defective tubular function such as concentrating ability, and decreased glomerular filtration rate with concurrent rises in serum creatinine. Due to the multifactorial causes of renal impairment it is not always easy to determine the contribution of these agents early in the course of therapy. However, renal toxicity clearly attributable to gentamicin is rarely seen before five days of treatment. Although animal experiments have suggested that tobramycin is less nephrotoxic than gentamicin clinical experience to date does not provide firm support for this view. Renal complications are more common in certain clinical settings. Among them are prolonged treatment, pre-existing renal disease, and older age group of the patient. Aminoglycoside doses that give prolonged elevated serum concentrations are more likely to cause renal damage and this may be reflected in both elevated peak and trough values.

Table I

Dosage of Aminoglycosides

	Expected Peak Serum Concentrations (ug/ml)	Initial Dosage (Mgm/kg) Child	Adult	Dosage Interval* (hrs)
Gentamicin and Tobramycin	4 - 10	1.7 - 2.3	1 - 2	8
Kanamycin and Amakacin	15 - 25	7.5	7.5	12

*For patients with normal renal function

Therapeutic Goals and use of Serum Concentrations

The relatively narrow therapeutic index of all aminoglycosides poses the greatest practical difficulties in using these drugs. One must use doses sufficient to achieve the desired curative antibacterial effects (see Table 1), yet use doses low enough to minimize the potential renal or eighth cranial nerve toxicities. Severe infections that are difficult to eradicate, such as serratia endocarditis or pseudomonas osteomyelitis, may require extremely aggressive therapy. In such cases it is necessary to use high doses of these agents and thus increase the risk of toxicity. The dose for initial therapy may be selected from the dosage schedule outlined in Table I. In patients with normal renal function subsequent doses of the aminoglycosides, if given at intervals of 8-12 hours, are identical to the first dose. This follows from the recognition that the serum half-life for these drugs is 2-4 hours in patients with normal renal function and thus administration of subsequent dosages at intervals of 3-4 half-lives does not result in significant accumulation. In patients with renal failure the dosage should be modified to avoid accumulation. This can be estimated by using any of several published guidelines.[16-18] However, in practice the most direct method of establishing the appropriate continued dosage of an aminoglycoside is to measure serum concentrations of the drug. Several types of assays have been described: bioassay, enzymatic drug conversion or radioimmunoassay. All are accurate if performed properly and in most hospitals at least one of these techniques is now available to the clinician. It is important for the laboratory to be aware of the concomitant use of other antimicrobials since their presence may give falsely elevated results.

Aminoglycoside serum concentrations are standardly drawn soon after ("peak") and immediately prior to ("trough") a drug administration. If the peak

Table II
Bacterial Inactiviating Enzymes

	Acetylation			Adenylation	Phosphorylation
Aminoglycoside	**AAC (2')**	**AAC(6')**	**AAC(3')-I**	**ANT (2')**	**Aph (2')**
Gentamicin	+	+	+	+	+
Tobramycin	+	+	+	+	
Kanamycin		+	+	+	
Amikacin		+			

AAC	Aminoglycoside acetyltransferase
ANT	Aminoglycoside adenyltransferase
APH	Aminoglycoside phosphotransferase

concentration is obtained one hour after the aminoglycoside is given (a half-hour after completion of an intravenous infusion or one hour after an intramuscular injection), the result will show concentrations after equilibration between the serum and extravascular compartments has occurred.[19] Although this value will be slightly lower than the highest concentration achieved immediately after an intravenous infusion it can be used more reliably to calculate the serum half-life of the drug. For patients with normal renal function peak and trough concentrations should be obtained three to five doses after initiating aminoglycoside therapy. Where coexisting renal insufficiency is present (i.e., acute oliguria or previously elevated serum creatinine) these samples should be obtained earlier. From these findings the need for adjustments in aminoglycoside dosage can be determined rationally. If adjustments are required the serum concentrations should be repeated to determine if the desired change has been obtained.

When satisfactory levels are confirmed repeat measurements are usually unnecessary unless changes in renal function occur. Thus in most patients with normal renal function a single set of aminoglycoside serum concentrations will be adequate, whereas in others whose renal function is impaired and/or changing acutely many determinations may be necessary to maintain values within the desired range.

Acquired Resistance

The most commonly encountered form of bacterial resistance to the aminoglycosides results from enzymatic inactivation by bacterial enzymes. As shown in Table II, the aminoglycosides vary in their sensitivity to the action of the five major bacterial enzymes. The genetic determinants for the enzymes are specified by plasmids (R-factors) that can be transferred from one bacterial strain to another, conferring aminoglycoside resistance on the recipient.[20] Of special importance clinically is the observation that R-factor mediated resistance can be transmitted between bacterial species, resulting in aminoglycoside resistance in more than one type of bacteria. A second type of resistance results from alterations in bacterial ribosomes such that they fail to bind the aminoglycoside(s). This is of clinical importance only with respect to streptomycin. A third type of resistance results from failure of the, bacterium to transport the aminoglycoside across the membrane. This results in sublethal intracellular concentrations of the drug. This form of resistance can occur for any aminoglycoside.

The development of aminoglycoside resistance has become a significant medical problem in the United States and has led to outbreaks of difficult-to-treat, serious nosocomial infections. Physicians should be aware of the current aminoglycoside sensitivities of gram-negative organisms in their hospitals because aminoglycoside resistance my vary markedly, depending in large measure on prior local community patterns of antimicrobial use. These data, rather than more general textbook recommendations, should form the basis for choice of aminoglycosides for presumed hospital-acquired infections due to gram-negative aerobic organisms.

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Internists:

Is That What We Are Turning Out

Part II

Last month's editorial dealing with community hospital training programs for internists raised some important points regarding medical training. In this editorial some suggestions are presented which perhaps, if implimented, can improve the situation.

It would appear that community hospitals cannot match the faculty of university centers either in scope or depth and therefore must settle for a different approach to the training of internists. Turning to fulltime clinicians for part-time help in teaching has been the mainstay of clinical training during rotations through many private and community hospitals for many of us "older" physicians. However, we always had the resource of the University when difficult diagnostic dilemmas occurred. Lacking this backup creates a problem for the community hospital. One way in which the local programs in Arizona could be strengthened would be to tie all the internal medicine training programs either tightly or loosely to the University of Arizona School of Medicine.

Once this is accomplished, I believe tying together of all training programs in a given locale would be an additional strengthening force. Not only would they be tied to the University, but they in addition would be tied to each other thus affording them additional support. Is there really a need to have three separate internal medicine residency programs at three separate hospitals? Is there not a redundancy of people and paperwork that occurs with such a setup? Wouldn't it be more advantageous to have a unified training program whereby the residents would rotate from hosptial to hosptial? Such a situation now exists in Phoenix, for instance, in pediatric training where a community wide program is in existence. Not only do the residents rotate to the various hospitals to see how medicine is practiced at community, Veterans Administration and County hospitals, but also the faculty at each of these institutions gains exposure to the residents which can only lead to improved teaching for the overall program.

The next logical step in the development of such programs would be to bring in more people to do the basic science and physical diagnostic teaching. This is the most radical of the thoughts contained within this editorial for it poses significant threats to practicing physicians in the community. The same "town versus gown" problems which surfaced in the past could again arise obliterating the input from the practicing physician. However, in major cities where such a situation exists, there appears to be ample precedent that would allow its success in Arizona. If the clinicians were given the opportunity to teach clinical medicine and the fulltime physicians concentrated on the underlying physiological principles relating to the practice of medicine, the best of two worlds would result.

I feel that the training in most Arizona programs could be improved. There are some who feel independant community hospitals should not be training internists while others feel it is the best method available. Neither side has yet adequately proven their points of view.

Marshall B. Block, M.D.
Editor

The Class of 1980:

Comments on Uniqueness

Each graduating class of medical students has a personality of its own. Characteristics of culture, ethnicity, age and sex are melded with career goals for each student. Beginning with the first basic science and clinical exercises, individuals evolve into a group influenced and guided as the education process takes place. Upon completion of the medical school experience, the graduates move from undergraduate to graduate experiences, leaving as a class whose "personality" is the unique mix of the individuals collectively receiving the M.D. degree.

Like most other graduating classes, the Class of 1980 has educational characteristics reflecting diverse premedical experiences. By a unqiue quirk of our recent change from a three-year to a four calendar year program, however, there will be a wide variation in these students' education for the first two years of medical school.

The students who graduated in the spring of 1979 entered the College no later than the summer of 1976, beginning a three-year curriculum. The next entering class began a four-year curriculum experience in the summer of 1977; their anticipated graduation is four years later—1981. The practical result of this change from three to four years of curriculum time is a space in the two years preceding 1980. This time space provided a special opportunity for additional students to study in clerkships and elective courses in our clinical programs. To that end it was arranged for a group of students to enter our College the fall of 1978 and begin almost 80 weeks of clinical clerkships and elective experiences, with expected graduation in the spring of 1980.

The class to graduate in 1980 is made up of some students from the previous class who chose to extend their three-year curricular experience to four years, plus students from other medical schools who have completed two or more years of medical education. The basic requirements of students wishing to transfer to Arizona was a minimum of successful completion of the usual premedical courses in an accredited U.S. university and passage of Part I of the National Board of Medical Examiners test.

Students transfer between medical schools for many reasons. Some wish to return to their home state from other U.S. medical schools; some U.S. born students wish to return to a U.S. school from foreign medical schools; other students must transfer to complete their clinical education after having attended a school offering only two basic science years. Because of this diversity, the class of 1980 has characteristics quite different from those of other classes. Of the 58 students now scheduled to graduate in 1980, approximately one-third are "extenders" from our three-year curriculum, one-third are transfers from foreign medical schools, and one-third are transfers from two-year medical schools.

This diversity of backgrounds has brought new challenges for the educational process. With the guidance of the College's Admissions and Curriculum Committees, a special educational program was designed to ensure the students have a standard preparation for clerkships. After pretests for basic knowledge in pathology and clinical skills, the students were advised of their level of achievement compared to our usual student entering clinical clerkships. Through classroom exercises, programmed patient/simulators, and patient/preceptor experiences, the Class of 1980 students reviewed and supplemented their existing knowledge and skills, and sometimes studied entirely new areas of clinical pathophysiology, approaches to clinical diagnosis, human behavior and development, and physical diagnosis skills. Each student was required to reach a predetermined level of achievement on post-testing. Upon completion of this special program, the Class of 1980 is entering clerkships at the same level of competence as other students in Arizona.

On entering the clinical years, the Class of 1980 has become a unique class—having a personality of its own, but assured of adequate preparation to advance through the clinical years with confidence.

Louis J. Kettel, M.D.
Dean, College of Medicine

Paula L. Stillman, M.D.
Curriculum Coordinator, Preparation for Clinical Medicine

Sarah M. Dinham, Ph.D.
Director, Office of Medical Education

Andrew M. Goldner, Ph.D.
Associate Dean, Student Affairs

Auxiliary Highlights Physicians' Families

Introducing the 1979-80 Auxiliary Highlights editor. . .
Mrs. John T. Clymer, Tucson, writes with editorial background and a vital motivation by virtue of also being the current state president of Auxiliary. She has many enthusiastic ideas for utilizing the considerable talents of Auxiliary members and will be reflecting those plans in her writings. Enjoy!
Mrs. Melvin W. (Jean) Phillips
Retiring Auxiliary Editor

One hundred fourteen physicians and spouses of doctors turned out in the early morning April 26 at the ArMA Annual Meeting to hear Drs. Ellen and Perry Berman discuss "Physicians' Families" and to talk in groups about some of their concerns and the ways they met stress.

The program was sponsored jointly by ArMA and the Auxiliary.

It was an exhilarating morning. The hour-and-a-half discussion period sped by. The groups were open and the talk was frank.

What did they discuss? Changing values, changing goals, changing rewards. . .
the physician's image today parent-child relationships the hard time of starting a medical practice . . . the stress of being a resident's wife, away from the extended family . . mid-life changes in careereconomic pressures . . . . .life in a small town . taking the time to talk with each other, taking time to be with each other.

There was general agreement that most doctors are compulsive "workaholics." Therefore it's important to plan time to be with the family, to learn to play, to use exercise as a means of winding down from stress. It may mean limiting a practice. It may mean facing the question of why the doctor feels more needed by patients than by his or her family.

Marriage needs to be worked at, said another group. At the office and hospital, the physician is expected to avoid intimate relationships and to keep things on a detached, professional level. The doctor's role is God-like, unassailable, not-to-be-questioned. It's a problem switching from the immortality of the hospital to the humanity of home. Doctors shouldn't be shielded from problems at home by the spouse. Doctors should share fully in the responsibility of child-rearing. Doctors should allow themselves to be more vulnerable, more imperfect, more human.

The spouse, on the other-hand, must remain an individual, growing and changing with the times. Hobbies, outside activities or a career are important. Looking ahead, anticipating change, planning to meet change is necessary.

These are some of the observations that came out of the morning meeting. But how do you describe the intensity of the discussions or the support members of the groups gave to each other?

Evaluation cards were virtually unanimous in asking for more such programs. In the meantime, we can hope that now we have begun to openly discuss our cares and concerns with our friends and colleagues, we will find it easier to talk with others at work, at church, at home.

Even the guest speakers learned something at this meeting. The Bermans said they had not realized before that the threat of a malpractice suit and the expense of malpractice protection was a source of stress not only for the physician but for his family.

The Auxiliary is grateful to the Association and to Drs. Marvin Schneider, Jim Hurley, and the other memebers of the Scientific Assembly Committee for their encouragement and support in the planning of the program and to Bruce Robinson for his help.

We also want to thank the Arizona psychiatrists who served as discussion leaders: Hal J. Breen, David S. Burgoyne, Murray M. DeArmond, James G. Hill, John Jarvis, Derald G. May, M.D. Sarah B. Nelson and Dennis C. Westin.

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John Stoner III, M.D.
William C. Weese, M.D.
Donald J. Ziehm, M.D.

ArMA Reports

THE MINUTES APPEARING IN THIS SECTION HAVE BEEN EDITED TO CONSERVE SPACE. A COMPLETE COPY OF THE MINUTES OF ANY MEETING WILL BE MAILED TO ANY MEMBER REQUESTING THEM.

Professional Committee

Meeting of the Professional Committee of the Arizona Medical Association, Inc., held at 810 West Bethany Home Road, Phoenix, Arizona, on Tuesday, April 13, 1979, convened at 7:28 p.m., Joseph W. Hanss, M.D., Chairman, presiding.

Section on Mental Health and Substance Abuse

Paul M. Bindelglas, M.D., reported that he met with representatives of the Arizona Recovery Centers Association. They would like to make presentations to Arizona physicians on recongnizing alcoholism in its early stages. They will contact Dr. Bindelglas when their presentations are prepared. RECEIVED FOR INFORMATION.

Section on Sports Medicine

William C. Brainard, M.D., reported that the Board of Directors referred to the Section on Sports Medicine a request from the Pima County Medical Society relating to pre-participation sports physical examinations. The Pima County Medical Society has endorsed a program in which pre-participation sports physicial examinations are required only prior to the first year of sports participation with injured and sick athletes being carefully followed and re-examined prior to returning to participation. This program has been adopted by the NCAA. Pima County Medical Society is seeking ArMA's endorsement of the program and adoption by the Arizona Interscholastic Association. The Section on Sports Medicine determined that the program has merit and they will support it. In addition, they will select several Maricopa County high schools to implement the same program on a pilot basis to further study the value of the continuation of such programs on a statewide basis.

It was noted that the Board of Directors has voiced acceptance of the plan of the Pima County Medical Society for their implementation of pre-participation sports physicals as approved by the Section on Sports Medicine. Therefore, no further action by the Board of Directors was considered necessary at this time. RECEIVED FOR INFORMATION.

Dr. Brainard reported that the 5th Annual Sports Medicine Symposium held in January was very successful. There were many prominent speakers and the program drew nearly 500 attendees. RECEIVED FOR INFORMATION.

Liaison to the Auxiliary

It was reported that the immunization bill, actively supported by the Auxiliary, has passed the Senate and is being heard in the House. The bill still lacks the mandatory provision originally requested, but is stronger than the previous bill. It was noted that the Auxiliary is doing a superb job in lobbying for this bill.

Section on Allied Medical Groups

Gary L. Barnett summarized the legislative activities of the allied medical groups, specifically the podiatrists, chiropractors, nurse practitioners, optometrists, and homepaths. It was noted that most of these bills are being held in the House Health Committee for review during the summer months in a specially appointed Joint Study Committee on Allied HeaLth Groups. Dr. DuPont will be very active with the study committee. RECEIVED FOR INFORMATION.

Section on Aging and General Medicine

Definition of Death

Robert L. Hagan, M.D. reported that the Section on Aging and General Medicine is continuing to work on a definition of death. They have reviewed model legislation received from the American Medical Association. RECEIVED FOR INFORMATION.

Biofeedback

Dr. Hagan presented a letter inquiring about the position of the Ariozna Medicial Assocation on the modality of biofeed back. It was noted that the Maricopa County Medical Society Foundation, the Pima County Medical Society Foundation and Blue Cross and Blue Shield do not presently recognize biofeedback as a modality for coverage under their payment plans. Attached with the letter was a brochure announcing an Open House at The Samaritan Stress Center for the purpose of discussing biofeedback. There was discussion.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATION NOT OBJECT TO THE MODALITY OF BIOFEEDBACK IN ITS CLINICAL USE IN A APPROPRIATE SETTING UNDER A PHYSICIAN'S SUPERVISION.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATION OBJECT TO BLATANT ADVERTISING OF SUCH MODALITIES AS BIOFEEDBACK WHICH PURPORT TO GIVE THE IMPRESSION THAT IT IS A CURE FOR ALL ILLS AND REFER SUCH ADVERTISMENTS TO THE COUNTY MEDICAL SOCIETY.

Section on Poison Control

Legislation was introduced to provide for a free standing poison control center at the University of Arizona. It was reported that this concept has been well accepted and the proposed legislation should pass during this legislative session. RECEIVED FOR INFORMATION.

SECTION ON HEALTH EDUCATION

Warren L. Niccum, M.D. reported that the American Red Cross and Central Arizona Health Systems Agency would be sponsoring a workshop to review the approach to health education dealing with self-health responsibility of the individual. The workshop will determine the role of the school in providing leadership and training in proper health habits so that students can be encouraged to take responsibility for improving and maintaining their own health. The preliminary response to the program from school nurses and administrators has been good. RECEIVED FOR INFORMATION.

Section on Emeregency Care and Disaster Medicine

The Committee received copy of and reivewed the "The Arizona Chapter, A.C.E.P., Official Standards for Minimal Requirements for Privately Owned Or Hospital Affiliated Free Standing Emergency Facilities" and the "Standards For Emergency Medical Facilities" adopted by Blue Cross and Blue Shield of Arizona, Inc. Board of Directors. Copies of both reports are on file at the Association headquarters. It was noted that the A.C.E.P. Standards are more rigid than those adopted by Blue Cross and Blue Shield. There was discussion.

IT WAS MOVED AND CARRIED TO RECOMMEND TO THE BOARD OF DIRECTORS THAT THE ARIZONA MEDICAL ASSOCIATION ADOPT AS THEIR STANDARDS FOR FREE STANDING EMERGENCY MEDICAL FACILITIES THE STANDARDS OF THE ARIZONA CHAPTER, AMERICAN COLLEGE OF EMERGENCY PHYSICIANS.

Other Business

Ban on Saccharin

The Committee received correspondence seeking the support and assistance of the Arizona Medical Association in preventing the ban on saccharin from occurring. It was noted that the moratorium on the FDA's proposed ban on saccharin will expire on May 23, 1979.

IT WAS MOVED AND CARRIED TO REFER TO THE SECTION ON PUBLIC HEALTH, CORRESPONDENCE SEEKING THE SUPPORT OF THE ARIZONA MEDICAL ASSOCIATION IN PREVENTING THE BAN ON SACCHARIN FROM OCCURING.

Medical Aid to Children

Joseph Hanss, M.D. brought to the Committee a "Consent to Emergency Treatment" from which he was asked to complete and sign for his children in school. This form would give permission of treatment in instances when the child is injured at school and the parents cannot be reached.

IT WAS MOVED AND CARRIED TO REFER THE "CONSENT TO EMERGENCY TREATMENT" FORM TO THE SECTION ON EMERGENCY CARE.

Continued from Page 456

Subcarinal Bronchogenic Cyst

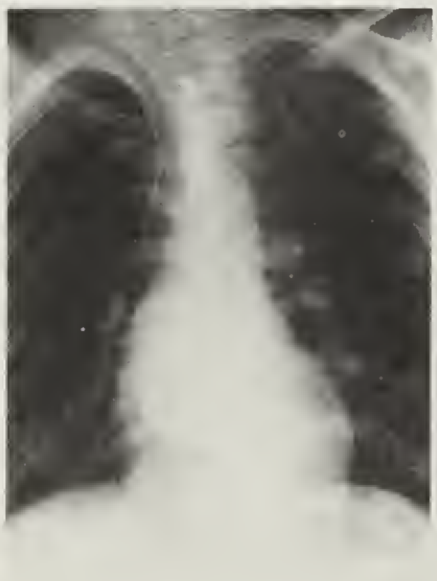

Figure 3

Although the patient's acute symptoms were secondary to an upper respiratory tract infection which subsequently spontaneously resolved, a large middle mediastinal mass was detected on the roentgen chest examination. The mass is visualized on the lateral radiograph (Figure III), as a homogenous oval density with sharply defined smooth borders which is located posterior to the heart, inferior to the carina, and posteriorly is limited by the antero-lateral aspects of the adjacent dorsal vertebrae. The frontal view of the chest (Figure I) deomonstrates the mass superimposed over the right border of the cardiac silhouette.

A follow-up esophagram (Figure III) demonstrated left lateral displacement of the mid-esophagus by an extrinsic pressure defect. The plain raidograph and fluoroscopic examinations demonstrated no evidence of thoracic bony abnormalities or esophageal infiltration nor communication with the mass. Although an unusual, clinically occult, primary or metastatic neoplasm could have a similar appearance, these finding are more suggestive of a benign etiology.

The most common etiology for such a subcarinal middle mediastinal mass is that of a foregut duplication cyst. These are congenital in origin and may be incidentally discovered in any age group. The respiratory tract and esophagus have a common embryological origin from the foregut. Bronchogenic cysts result from an abnormal accessory budding or branching of the tracheo-bronchial tree, either before or after embryologic separation from the foregut anlage. For this reason, the cysts are classified under the general category of "foregut duplication cysts". This term is inclusive of enteric cysts, which are congenital lesions, arising from the aberrant development of the gastroentestinal portion of the foregut. These have similar radiographic features and usually cannot be distinguished from either bronchogenic or neurenteric cysts until surgical exploration. Although the bronchogenic cysts are located in close proximity to the trachea or bronchi, the majority demonstrate no communication with the actual lumen of the tracheobronchial tree. However, when there is communication, prominent air-fluid levels may be visualized within the cyst.

Clinically, the symptoms associated with these cysts are variable and depend on the size and location of the cyst. Although hilar and subcarinal locations are most common, occasionally the cyst may be either in a right para-tracheal or para-esophageal location. Usually, as in this case, bronchogenic cysts are initially detected as incidental discoveries on routine or baseline chest radiography. However, these cysts may increase in size due to the accumulation of products secreted by mucous glands lining the mucosa. As a result of such increased volume, or growth, the patency of adjacent bronchi may be compromised resulting in atelectasis and/or recurrent respiratory tract infections with related symptoms of thoracic pain, cough, or wheezing.

When the bronchogenic cysts are discovered in infancy, the predominant location is subcarinal. Cysts in this location often cause severe respiratory obstruction secondary to carinal airway compression. Unfortunately, this variety of cysts is difficult to detect radiographically, since the soft-tissue of the surrounding mediastinum silhouettes the margins of the lesion. Therefore, a high of suspicion for the diagnosis is required when an infant presents with clinical evidence of severe obstructive respiratory symptoms and with concurrent radiographic signs of airway obstruction, such as asymmetric air-trapping or retained fetal lung fluid. An esophagram is essential in establishing the tentative diagnosis, since most cysts are large enough to cause an extrinsic pressure defect on the esophagus.

In this patient, a large ovoid cyst filled with thick mucoid material was excised at thoractomy. Micropathologically, the cyst was lined by respiratory-like columnar ciliated epithelium and demonstrated submucosal elements characteristic of bronchogenic cyst, *i.e.*, mucous glands, cartilage, and smooth muscle fibers. The patient had an unremarkable post-operative course.

References

1. Eraklis AJ, Griscom NT, McGovern JB: Bronchogenic cysts of the mediastinum in infancy. *New Eng J Med* 281(21):1150-1155, 1969.
2. Maier HC: Bronchogenic cysts of the mediastinum. *Annals of Surgery* , 127:476-502, 1948.
3. Opsahl T, Berman EJ: Bronchogenic mediastinal cysts in infants: Case report and reivew of the literature. *Pediatrics*, 30:372-377, 1962.
4. Reed JC, Sobonya RE: Morphologic analysis of foregut cysts in the thorax. *Am J Rotegenol*, 120(4):851-860, 1974.
5. Salyer DC Salyer WR, Eggleston JC: Benign developmental cysts of the mediastinum. *ARch Pathol Lab Med*, 101:136-139, 1977.

Future Medical Meetings

CONTINUING MEDICAL EDUCATION

The following institutions and organizations have been accredited for their continuing medical education programs by the Liaison Committee on Continuing Medical Education.

Arizona Heart Institute
Arizona Medical Association, Inc.
Arizona State Hospital, Phoenix
Camelback Hospital, Phoenix
Desert Samaritan Hospital, Mesa
Good Samaritan Hospital, Phoenix
Health Maintenance Associates, Phoenix
Maricopa County General Hospital, Phoenix
Mesa Lutheran Hospital, Mesa
Phoenix Baptist Hospital & Health Center
Phoenix Indian Medical Center
Phoenix Memorial Hospital
Phoenix Psychiatric Council
St. Joseph's Hospital & Medical Center, Phoenix
Barrow Neurological Institute, Phoenix
St. Lukes's Hospital & Medical Center, Phoenix
Scottsdale Memorial Hospital
Tucson Hospitals Medical Education Program, Tucson
Veterans Administration Hospital, Phoenix
Veterans Administration Hospital, Prescott
University of Arizona College of Medicine, Tucson

The accredited institutions and organizations above produce a variety of continuing medical education programs. Each accredited institution and organization is responsible for designating which of these programs meet ArMA's requirements for Category 1 credit. Physicians who participate in programs which are designated Category 1 by accredited institutions will receive Category 1 credit toward the ArMA Certificate in CME and tne AMA's Physician's Recognition Award.

JUNE

Advanced Cardiac Life Support - Provider
June 22 & 23, 1979. Arizona Medical Association offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner, ArMA Offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Approved for 16 hours of category 1 credit.

JULY

22nd Annual Ruidoso Family Practice Seminar
July 16-19, 1979. Inn of the Mountain Gods, Mescalero, New Mexico. Sponsor: New Mexico Chapter of the American Academy of Family Physicians. Contact: Bob Reid, Chairman, P.O. Box 456, Sunland Park, N.M. 88063. Approved for CME credit hours.

Advanced Cardiac Life Support Program - Provider
July 20 & 21, 1979. Arizona Medical Association offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Sponsor: Arizona Affiliate of the American Heart Assoc. Contact: Carol Turner, ArMA Offices, 810 W. Bethany Home Rd., Phoenix, AZ 85013. Approved for 16 hours of category 1 credit.

Summer Medical Seminar
July 28-29, 1979. Little America, Flagstaff, Az. Sponsor: The Coconino County Medical Society. Contact: Thomas Davee, M.D., 710 N. Beaver St., Flagstaff, AZ 86001. Approved for 8 hours Category 1 credit.

A Day of Surgery
July 27, 1979. Little America, Flagstaff, Az. Sponsor: The Arizona Chapter of the aemrican College of Surgeons. Contact: Herbert Fredell, M.D., 120 W. Fine Ave., Flagstaff, AZ 86001. Phone: (602) 774-2491. Approved for 5 hours of Cateory 1 credit.

OCTOBER

Eighth Annual Symposium of the Western Division of the American Geriatrics Society
October 26-27, 1979. Lakes Club, Sun City Arizona. Sponsor: University of Arizona College of Medicine and Walter O. Boswell Memorial Hospital. Contact: Julius Schwimmer, M.D., 13220 105th Ave. Bldg. B, Rm. 61, Sun City, AZ 85351.

NOVEMBER

27th Annual Meeting of the Medical Society of the United States and Mexico
November 14-17, 1979. Doubletree Inn, Tucson, Az. Sponsor: Medical Society of the United States and Mexico. Contact: Mrs. Carolyn Parsons, Executive Secretary, 3161 N. Pantano Road, Tucson, AZ 85715.

MONTHLY OR WEEKLY

Shrine Medics Meeting
Second Tuesday of each month, Doctors Hospital, 5:45 p.m. J. South Classroom. Sponsor: Shrine Medics. Contact: Robert C. Briggs, M.D., 5121 N. Central Ave., Phoenix, AZ 85012.

Office Psychiatry for the Primary Provider
2nd Monday of month, 4811 N. 7th Street, Phoenix, AZ. Sponsor: Arizona Health Plan. Contact: T.R. Bittker, M.D., Box 5000, Phoenix, AZ 85010. Approved for category 1 credit.

Counter Transference Group
Weekly, Thurs. 8—10 p.m. Sponsor: Phoenix Psychiatric Council. Contact: James E. Campbell, M.D., 5051 N. 34th St., Phoenix, AZ 85018. Approved for 2 hours category 1 credit.

Monthly Meeting of Tucson Radiologists
Last Tues. of month. Plaza International, Tucson, AZ. Sponsor: U of A Medical Center, Dept. of Radiology. Contact: Irwin M. Freundlich, M.D., U of A Health Sciences Center, Dept. of, Radiology, Tucson, AZ 85724. Approved for 2 hours category 1 credit.

Pediatric Grand Rounds
Tuesday 7:30-8:30 a.m in Phoenix: 1st Tues.—Phoenix Indian Hospital, 2nd Tues.—Maricopa County Hospital, 3rd Tues.—Good Samaritan Hospital, 4th Tues.—St. Joseph's Hospital. Sponsor: Maricopa County Hospital (Phoenix Hospital's Affiliated Pediatric Program). Contact: J. Kipp Charlton, M.D., 2601 E. Roosevelt, Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

Review of Forensic Pathology Current Case, Special Topics
Thursday, weekly, 11 a.m., 120 S. 6th Ave., Phoenix, AZ. Sponsor: Arizona Society of Pathologists. Contact: H.H. Karnitschnig, M.D., 120 S. 6th Ave., Phoenix, AZ. Approved for 1 hour per session category 1 credit.

Staff Education Conference
Wednesdays, weekly, 1 p.m., Arizona State Hospital, Phoenix, AZ. Sponsor: Arizona State Hospital. Contact: Howard E. Wulsin, M.D., Arizona State Hospital, 2500 E. Van Buren, ·Phoenix, AZ 85008. Approved for 1 hour per session category 1 credit.

BARROW NEUROLOGICAL INSTITUTE

Medical Education
Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013. Sponsor: St Joseph's Hospital & Medical Center. Contact: John R. Green, M.D. Approved for 1 hour category 1 credit.

Neurology Teaching Conference
Tuesdays, 8:30-9:30 a.m., Eighth Floor Conf. Room.

Neurosurgery Morbidity Conference
Wednesdays, 8:15-9:15 a.m., on first and third weeks, Eighth Floor Conference Room.

Neuro-ophthalmology Conference
Tuesdays, 7:30 a.m. in 8th floor neurology conference room.

Spinal Injury Conference
Wednesdays, 8:15-9:15 a.m., on second and fourth weeks, in Neuropathology Conf. Rm.—a multidisciplinary review of admission by neurosurgeons, orthopedists, and rehabilitation specialists

Neuropathology of Gross Specimens Conference
Thursday, 7:30-8:30 a.m. in the Morgue.

Neurology-Neurosurgical Clinical-Neuroradiological and Neuropathological Conference
Fridays, 8-9 a.m., First Floor Conference Rm.

Neuropathology or Neuroradiology Conferences
Friday, 9 a.m., Neuropathology in Neuropathology Conference Rm., Neuroradiology in First Floor Conference Rm.

Neurorehabilitation Conference
Tuesdays, noon, 8th Floor Conference Rm.

Neurosurgical Journal Club
Saturdays, 9-11 a.m. in Eighth Floor Conference Rm.

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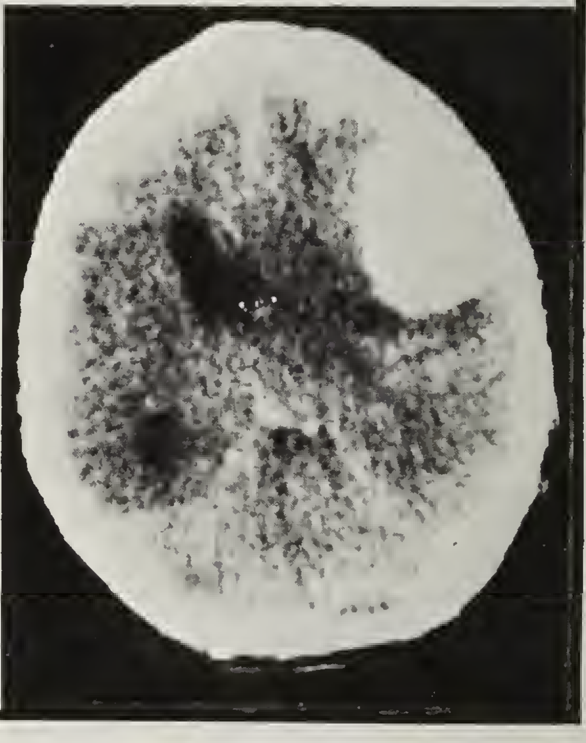

CAMELBACK HOSPITAL

5055 N. 34th St., Phoenix, AZ 85018. Sponsor: Camelback Hospital. Contact: Medical Director.

Patient Staffing Conference
Three times weekly.

DESERT SAMARITAN HOSPITAL

Wednesday evenings, 7 p.m. Sponsor: Desert Samaritan Hospital. Contact: L. A. Rosati, M.D., Laboratory, Desert Samaritan Hospital, Mesa, AZ 85202. Approved for category 1 credit.

GOOD SAMARITAN HOSPITAL

Clinical Cancer Conference
3rd Wednesday, every month, Butler Bldg. Conference Rm. Good Samaritan Hospital. Contact: John A. Bruner, M.D., 926 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour per session category 1 credit.

Pulmonary Disease Grand Rounds
Mondays, 12 Noon, D-5 North Conf. Rm., Good Samaritan Hospital, Phoenix, AZ. Sponsor: Pulmonary Disease Teaching Service, Good Samaritan Hospital. Contact: Bernard E. Levine, M.D., Pulmonary Function Laboratory, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix, AZ 85006. Approved for 1 hour category 1 credit.

MARYVALE SAMARITAN HOSPITAL

Continuing Medical Education Program
Maryvale Samaritan Hospital, every other Wednesday, 7-8 a.m., January 25, 1978

MARICOPA COUNTY GENERAL HOSPITAL

2601 E. Roosevelt, Phoenix, AZ 85008. Sponsor: Maricopa County General Hospital. Contact: H. F. Lenhardt, M.D., Dir. of Medical Education. Approved for category 1 credit.

The Hand Surgery Conference
Wednesday 7:30 a.m., Santa Cruz Room, Maricopa County Hospital.

MEMORIAL HOSPITAL

1201 S. 7th Ave., Phoenix, AZ 85036. Sponsor: Memorial Hospital. Approved for category 1 credit.

Month Medical Education Seminar
Third Monday, 6:30 p.m., Kiva Conference Rm. Contact: George Scharf, M.D.

Tumor Board Conference
Every Friday at Noon, Kiva Conference Rm. Contact: Howard Kimball, M.D.

SCOTTSDALE MEMORIAL HOSPITAL

7300 E. 4th St., Scottsdale, AZ 85251. Sponsor: Scottsdale Memorial Hospital. Contact: W. S. Wiliams, M.D., Director of Medical Education

Clinical Pathological Conference
4th Monday, monthly, 12:45 p.m.

Family Practice Conference
1st Monday, monthly, 12:45 p.m.

Medical Grand Rounds
3rd Monday, monthly, 12:45 p.m.

Morbidity & Mortality Conference
2nd Monday, monthly, 12:45 p.m.

ST MARY'S HOSPITAL & HEALTH CENTER

1601 W. St. Mary's Rd., Tucson, AZ 85703. Sponsor: St. Mary's Hospital & Health Center. Contact: see below.

Cardiology Conference
Every Friday 8-9 a.m., Century Rm. A. Contact: Anthony L. Forte, M.D.

Monthly Specialty Conference of the Department of Surgery
First Monday, monthly, 7:30 a.m. Century Rm. A. Contact: Medical Staff Office. Approved for 1 hour of category 1 credit

Grand Rounds: Medical Surgical, Family Practice, Pathology, Radiology
Weekly, Thursday, 7-8:30 a.m. Contact: Richard A. Silver, M.D. Approved for 1 hours of category 1 credit.

U OF A HEALTH SCIENCES CENTER

Sponsor: U of A College of Medicine, Tucson, AZ 85724. Contact: See below. Approved for category 1 credit.

Clinical Immunology, Allergy & Rheumatology Rounds
Every Friday, Noon-1 p.m. Contact: John Boyer, M.D., Dept. of Internal Medicine.

Cerebrovascular Disease Conference
Mondays, 5-6 p.m., weekly, Rm. 5505. Contact: Wesly Moore, M.D.,Depts. of Surgery, Nurology & Radiology.

Dean's Clinical Rounds
Contact: Louis J. Kettel, M.D.

Endocrinology Seminar
Every Thursday, Noon-1 p.m., 1st, 3rd & 5th Thursday, Room N318, VA Hospital. 2nd & 4th Thursday, Room 6505, Tucson Medical Center. Contact: Dept. of Internal Medicine.

Hematology-Oncology Clinical Conference
Every Tuesday, Noon-1 p.m., 1st, 3rd & 5th Tuesdays, Rm 6505, Tucson Medical Center. 2nd & 4th Tuesdays, Rm. N318, VA Hospital. Contact: Sidney Salmon, M.D., Dept. of Internal Medicine.

Joint Thyroid Clinic Conference
1st & 3rd Mondays of every month. 1 to 2 p.m., AHSC, Rm. 6505. Contact: Sidney Werner, M.D., Dept. of Internal Medicine, Endocrinology Section.

Medical Grand Rounds
Every Wed., Noon-1p.m., 1st, 3rd, & 5th Wed., Staff Conf. Room, VA Hospital. 2nd & 4th Wed., Rm. 5403, UAHSC. Contact: Jay Smith, M.D., Dept. of Internal Medicine.

Nuclear Medicine
Thursday, 7:30 a.m., Radiology Conf. Rm., UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Diagnostic Radiology.

Neurology Grand Rounds
Every Friday, Noon, 1st, 3rd, & 5th Fridays, UAHSC, Rm. 7505. 2nd & 4th Fridays, VA Hospital. Contact: William A. Sibley, M.D., Dept. of Neurology.

Neuropathology Review Conference
Thursdays, 8:30 a.m., Rm. 5120, UAHSC. Contact: Peter C. Johnson, M.D.

Neurosciences Seminar
Every Friday, 7:30 a.m.,UAHSC, Rm 7505. Contact: Colin R. Bamford, M.D., or Jose F. Laguna, M.D., Dept. of Neurology.

Pathology Seminar
Friday, 4:30-5:30 p.m., Rm. 5120, UAHSC. Contact: Paul Finley, M.D., Dept. of Pathology.

Tucson Pathologist Conference
First Monday of the Month, 7:30-9 p.m. Rotation between Tucson Pathology Conf. Rms. Contact: Anna Graham, M.D., Tucson Pathologists.

Pediatric Grand Rounds
Every Tuesday, 12:30-1:30 p.m. Alternates between Tucson Medical Center & UAHSC. Contact: Hugh Thompson, M.D., Dept. of Pediatrics.

Problem Case Workshop
3rd Monday of each month, 7:30 a.m., Rm 4410, UAHSC. Contact: H. E. Cross, M.D., Ph.D., Div. Of Ophthalmology.

Psychiatric Grand Rounds
Every Wednesday, Sept. to May 4, 5:30 p.m., Rm8403 UAHSC. Contact: Alan Levenson, M.D., Dept. of Psychiatry.

Chest Radiology
Monday, 5-6 p.m., weekly, Rm 1535F, UAHSC. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Gastrointestinal Radiology
Mondays, 7:30 a.m., weekly except for summer months. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Radiation Oncology Planning Conference
Friday, weekly, 8:30-10 a.m., UAHSC, Rm. 0655. Contact: Robert S. Heusinkveld, M.D., Radiation Oncology Section.

Radiology-Rheumatology Conference
Thursday, 8 a.m., UAHSC, Library Rm.1535C. Contact: Irwin M. Freundlich, M.D. Dept. of Radiology.

Vascular Radiology
Radiology Interesting Case Conference
Thursday, Noon, VA Hospital. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology.

Resident's Conference
Wednesday, weekly 5-6 p.m., Diag. Radiology Conf. Rm. Contact: Irwin M. Freundlich, M.D., Dept. of Radiology

Trauma Conference
Every Thursday, 4-5 p.m. UAHSC, Rm. 5505. Contact: Martin Silverstein, M.D., Dept. of Surgery.

Grand Ward Rounds—Trauma
Every Tuesday, 8 a.m., UAHSC. Contact: Martin Silverstein, Surgery Dept., Trauma Section.

Monthly Meeting Tucson Ultrasonography Group
First Wed. of month, 4:30-5:30 p.m., UAHSC. Contact: Irwin M. Freundlich, M.D.

Tucson Urological Society Scientific Meeting
Monthly. Contact: George W. Drach, M.D., Depts. of Surgery & Urology.

General Urology Conference
Tuesday 5-6 p.m. Thursday, Noon-1:30 p.m. UAHSC Meeting Rooms & VA Hospital. Contact: George W. Drach, M.D., Dept of Surgery/Urology Section.

VETERANS ADMINISTRATION HOSPITAL

7th St. and Indian School Rd., Phoenix, AZ 85012. Sponsor: VA Hospital. Contact: CME Department approved for Category 1 credit.

Academic Surgery Conference
Each Thursday — 2 p.m. — C435, Dr. Cannon, Ext. 493.

Cardiology Conference
2nd Thursday — 1 p.m. — T5, Dr. Habibzadeh, Ext. 348.

Cancer Symposium
Each Wednesday — 1 p.m. — T5, Dr. Berkley, Ext. 419.

Clinical Conference
4th Thursday of 3rd Month, (Mar. Jun., Sept., & Dec.), 1 p.m. — T5, Dr. Likos, Ext. 623.

Dermatology Conference
1st, 2nd, & 3rd Wednesday (usually, but is subject to change) 10 a.m. — C118, Dr. Roberts, Ext. 426.

G.I. Radiology Clinical Correlation Conference 1st & 3rd Monday —1 p.m. — C435, Dr. Sanowski, Ext. 618.

G.I. Grand Rounds
Ech Tuesday — 1 p.m. — T5, (4th Thursday with U of A Consultants) Dr. Sanowski, Ext. 618.

Medical Service Grand Rounds
Each Friday — 11 a.m. — T5, Dr. Zeller, Ext 272

Medical-Surgical Chest Conference
1st and 3rd Thursday — 1 p.m. — T5, Dr. Chowdhury, Ext. 388.

Medical-Surgical G.I. Conference
Ist & 3rd Friday — 2 p.m. — 2123, Dr. Sanowski, Ext. 618.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery Grand Rounds
Thursday — 3 p.m. Rm. C-435.

Surgery-Pathology Conference
Each Thursday — 2 p.m. — 2128, Dr. Cannon, Ext 493, & Dr. Likos, Ext. 623.

Urology-Pathology Conference
Each Wednesday — 7 a.m. — 2128, Dr. Likos, Ext. 623 & Dr. Pentenney, Ext., 417.

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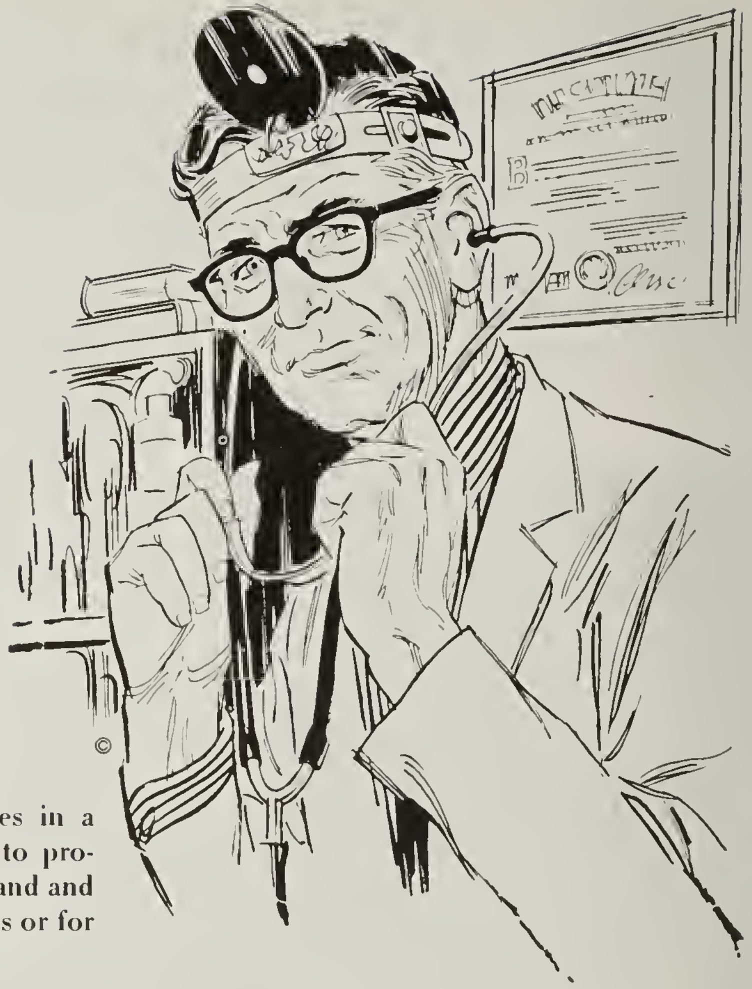

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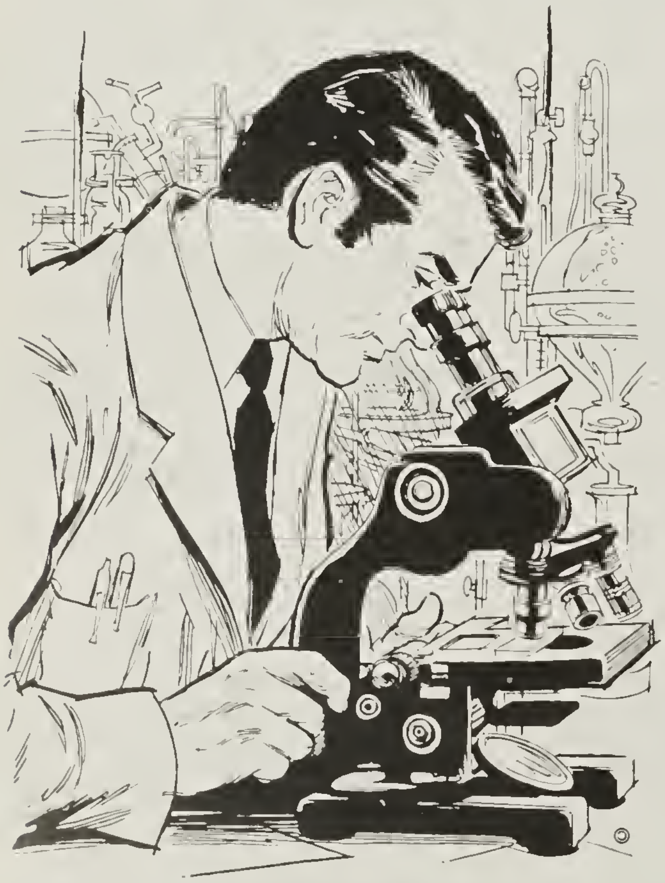
LOWER INSURANCE AGE: Often, one insured is somewhat younger than the other. The joint equal age can take years off the age of the older insured. The policy provides for the payment of the face amount upon the death of the first of the two insureds to die.

GUARANTEES SURVIVOR INSURABILITY: The surviving insured, within 90 days and prior to age 70, is guaranteed the right to purchase life insurance. If the surviving insured doesn't exercise this right and dies during this 90-day period, the conversion would automatically be made by the Company and the face amount, less the conversion premium, would be paid to his beneficiary.



DOUBLE FOR SIMULTANEOUS DEATH: If both insureds should die simultaneously, the sum insured upon their deaths would be paid to their beneficiaries.

CONVERTIBLE TO SINGLE LIFE: The Joint Life Insurance may also be converted to single insurance prior to the older insured's 60th birthday. The amount converted can be all on one life or the other or divided between the two as long as each does not take less than $1,000 of life insurance.

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INDICATIONS: *Therapeutically,* (as an adjunct to systemic therapy when indicated), for topical infections, primary or secondary, due to susceptible organisms, as in: infected burns, skin grafts, surgical incisions, otitis externa; primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia); secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis); traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically,* the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: This product is contraindicated in those individuals who have shown hypersensitivity to any of its components. Do not use in the eyes or in the external ear canal if the eardrum is perforated.

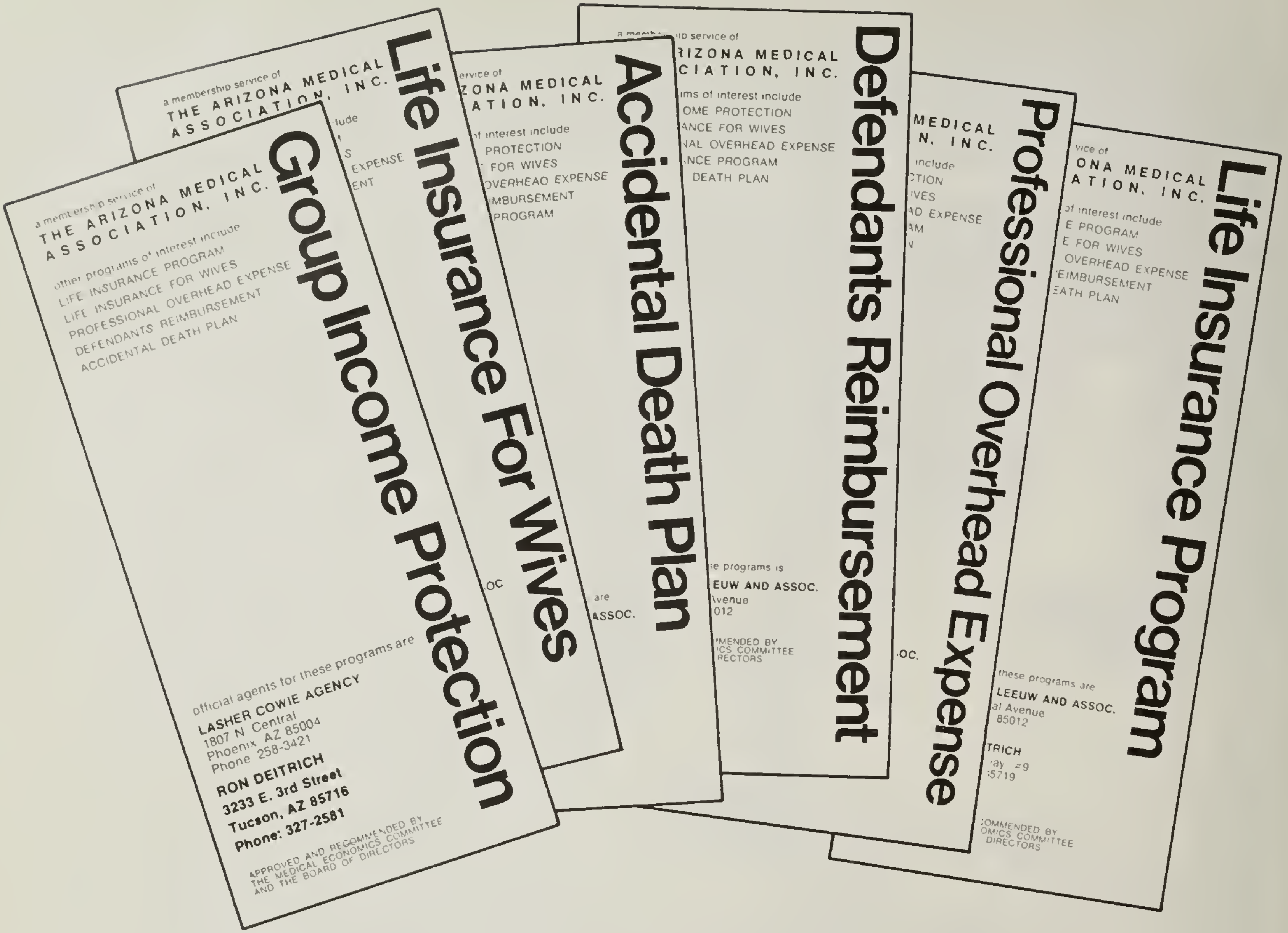
WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



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In Hypertension

As the hydrochlorothiazide in 'Dyazide' lowers blood pressure, the triamterene component limits potassium loss.

Serum K⁺ and BUN should be checked periodically particularly in the elderly, diabetics, and those with suspected or confirmed renal insufficiency (see Warnings). If hyperkalemia develops, substitute a thiazide alone.

Before prescribing, see complete prescribing information in SK&F Co. literature or *PDR*. A brief summary follows:

* **WARNING**
This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K⁺ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K⁺ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

Precautions: Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K⁺ frequently; both can cause K⁺ retention and elevated serum K⁺. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in postsympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules, Single Unit Packages of 100 (intended for institutional use only).

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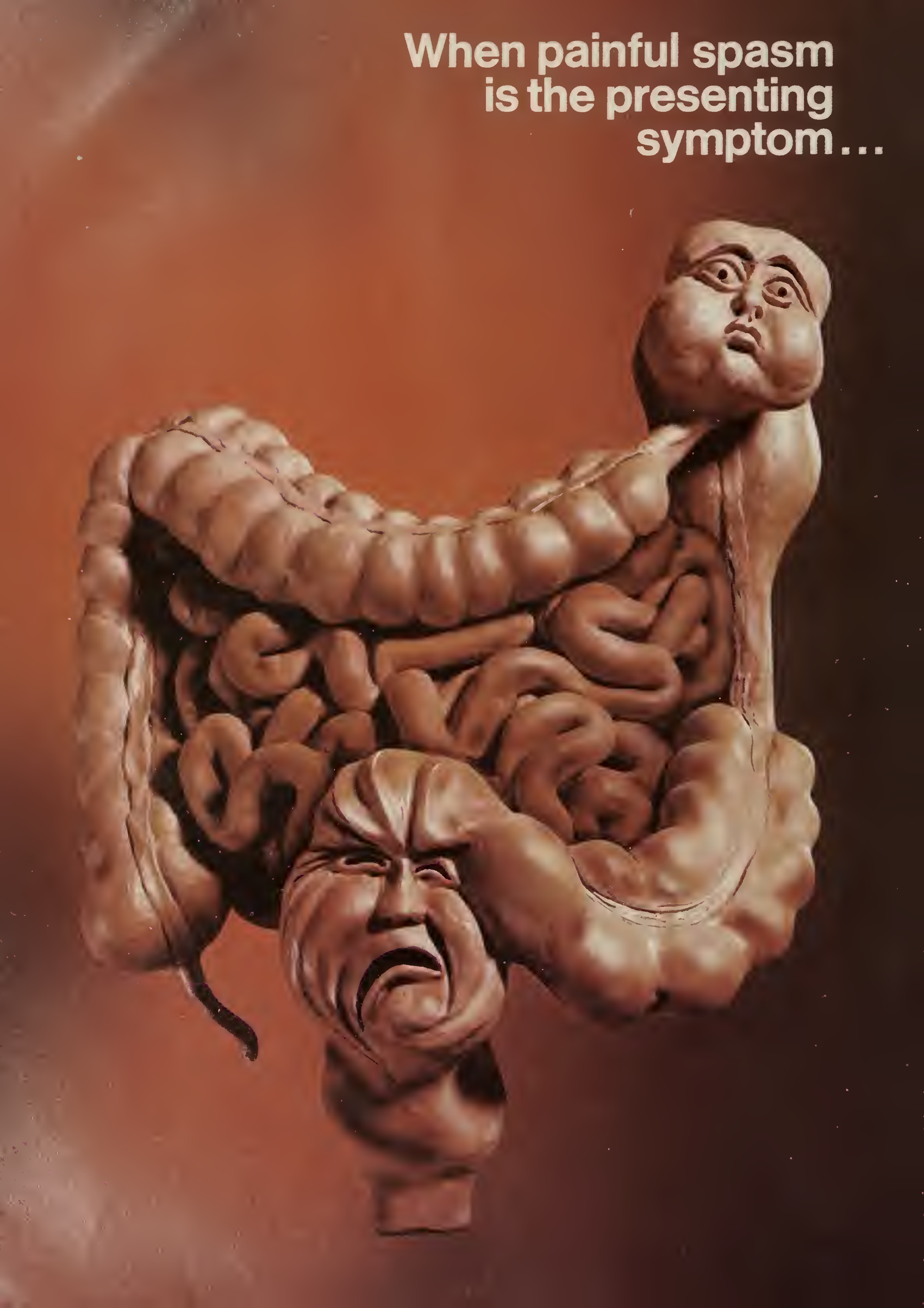
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...in the functional bowel/irritable bowel syndrome*

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. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.

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"The correlation of spasm relief and drug given was excellent."

*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:
King, J.C. and Starkman, N M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964

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Brief Summary

INOICATIONS
Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FOA has classified the following indications as "probably" effective

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis

THESE FUNCTIONAL DISDRDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION DF ENVIRONMENTAL FACTORS

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation

CONTRAINOICATIONS: Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis WARNINGS In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating) Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug PRECAUTIDNS Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy Use with caution in patients with. Autonomic neuropathy Hepatic or renal disease. Ulcerative colitis Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition

Do not rely on the use of the drug in the presence of complication of biliary tract disease Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate With overdosage, a curare-like action may occur AOVERSE REACTIONS: Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention, blurred vision and tachycardia, palpitations, mydriasis; cycloplegia, increased ocular tension, loss of taste, headache nervousness, drowsiness, weakness, dizziness; insomnia, nausea, vomiting, impotence, suppression of lactation, constipation bloated feeling severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations, some degree of mental confusion and/or excitement, especially in elderly persons, and decreased sweating With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. DDSAGE AND ADMINISTRATION Dosage must be adjusted to individual patient's needs.

Usual Dosage Bentyl 10 mg capsule and syrup. *Adults* 1 or 2 capsules or teaspoonfuls syrup three or four times daily *Children* 1 capsule or teaspoonful syrup three or four times daily *Infants* ½ teaspoonful syrup three or four times daily (May be diluted with equal volume of water.) Bentyl 20 mg *Adults* 1 tablet three or four times daily Bentyl Injection *Adults* 2 ml (20 mg) every four to six hours intramuscularly only NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE The signs and symptoms of overdose are headache nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.

Product Information as of October, 1978

Injectable dosage forms manufactured by CONNAUGHT LABDRATORIES, INC Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Decatur, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc. Cincinnati, Ohio 45215, U S A

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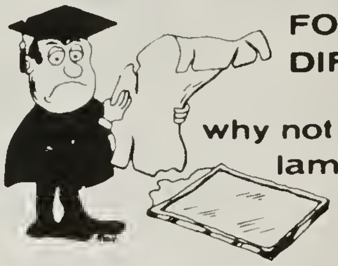
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